APRIL, 1953

The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

SYMPOSIUM ON DISEASES OF THE LIVER

Histologic Criteria for the Differential Diagnosis of Liver Diseases

The Present Status of Liver Function Tests

Liver Biopsy

•

Eighteenth Annual Convention

Los Angeles, Calif., 12, 13, 14 October 1953

VOLUME 20 NUMBER 4

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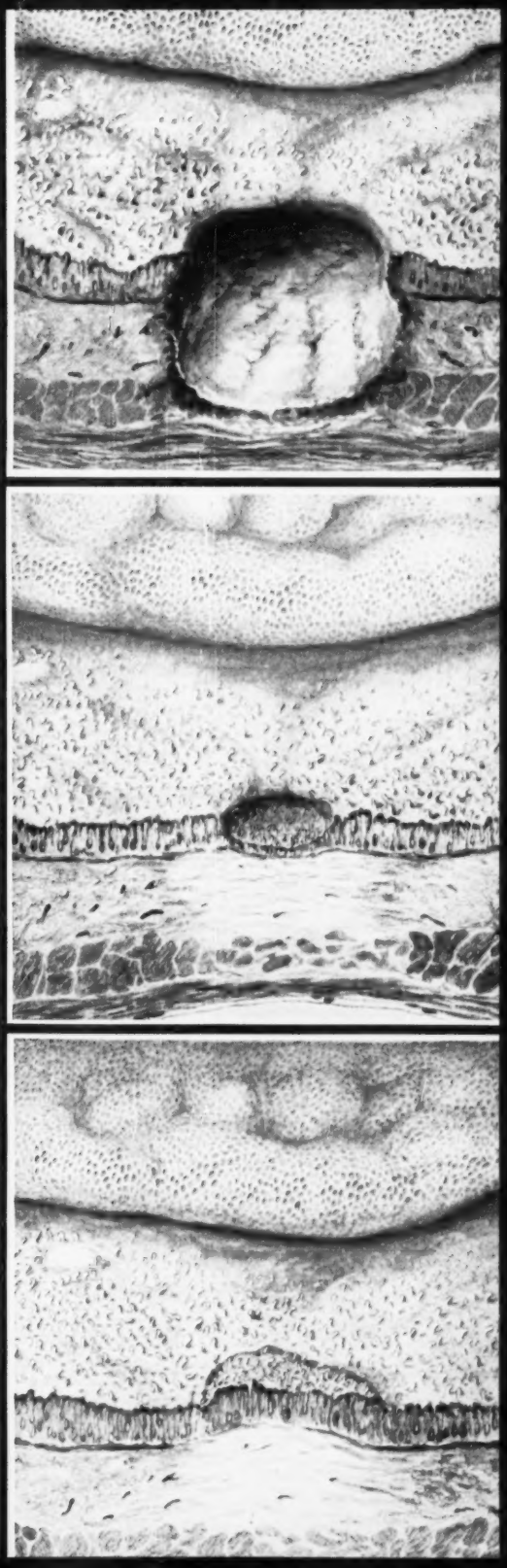

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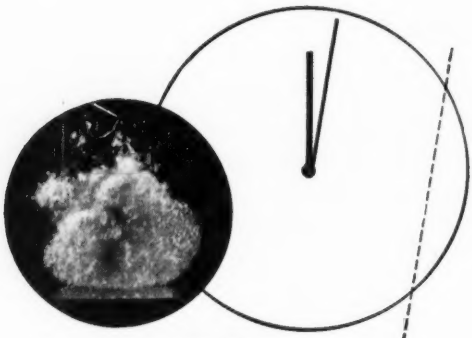

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The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

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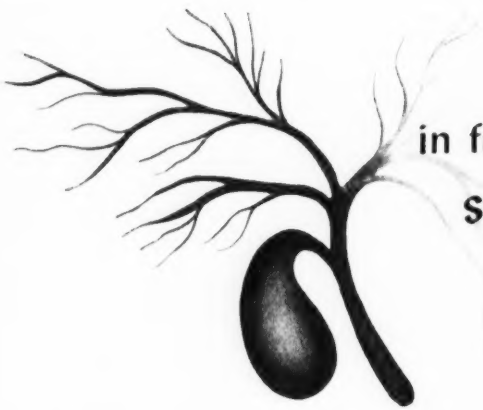

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The Review of Gastroenterology

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Volume 20 APRIL, 1953 Number 4

SYMPOSIUM ON DISEASES OF THE LIVER

LIVER BIOPSY*

JOHN R. NEEFE, M.D.
Philadelphia, Pa.

I am very grateful for the privilege of speaking to you this morning. My subject has the simple title, "Liver Biopsy". I think it would be generally accepted for one to make a statement that liver biopsy can now be regarded as an indispensable aid in the modern diagnosis and management of certain diseases of the liver and biliary tract.

In addition to specific liver diseases, this procedure also has proved to be of considerable value in the diagnosis of certain systemic diseases which elude a positive diagnosis by the multiple other methods available to us.

I regret that I have very little in the way of original material or new information to present to you. There have been many papers in recent years on this subject dealing with various aspects of the problem and describing in detail the technics employed. It would seem as though the most that I can do this morning is attempt to appraise the current status of this procedure and then to cite a few illustrations in which this procedure has been of particular value to us in our studies of certain clinical problems of the liver and biliary tract.

There are three methods of liver biopsy. The first, that of direct surgical biopsy, has been utilized for many years. If it is known that the patient is to be subjected to exploratory laparotomy in spite of what one might otherwise do, there is little point in consideration of a needle biopsy of the liver.

We must be cautious about the use of needle biopsy and I am sure that it has, like any new tool, very often been utilized in situations where it would not possibly influence the management of the patient. Many times when one knows that surgery is inevitable, there is little point in preceding the surgical procedure by a needle biopsy.

*Read before the Seventeenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 20, 21, 22 October 1952.

Another method with certain advantages is biopsy associated with peritoneoscopy. Perhaps the greatest disadvantage of this procedure is the lack of well trained peritoneoscopists. With men who are well versed in this procedure, there are certain advantages to taking the biopsy under direct observation, under conditions less drastic than direct surgical biopsy. Many patients who could not tolerate an exploratory laparotomy are quite satisfactory risks for the procedure of peritoneoscopy. I am sure there are many instances where peritoneoscopy and biopsy would be of great value and I personally believe the procedure is not utilized adequately in most institutions; however, I think there is little point this morning in discussing these particular methods further.

We shall proceed then to the third method, needle biopsy, which is the most simple and direct approach, in many instances, to specific diagnosis.

There are certain obvious and direct advantages of needle biopsy. First, it requires only a minimum period of hospitalization. No one today should undertake this procedure in the home or office as it can be carried out with only a 24-hour period of hospitalization. Generally speaking, it is relatively economical for the patient, and in the majority of instances, when properly done, there is relatively little discomfort. There are occasional patients who have considerable postbiopsy abdominal discomfort for a brief period, but, with proper local anesthesia and care, it is surprising how many have no pain or discomfort at all.

In many instances, needle biopsy affords an adequate specimen to permit a specific diagnosis with minimal risk. Patients with obvious contraindications are excluded.

There are certain limitations of needle biopsy. It is obvious that it is essentially a blind procedure. One does not know what area of the liver is being sampled. It is used most frequently, however, in diffuse diseases of the liver and it is surprising how often one gets a representative picture of the total process as compared with subsequent postmortem evaluation.

In localized diseases such as metastatic lesions, where they are infrequent, or with single localized lesions, obviously one is very likely to miss an area of pathology. The small sample is another disadvantage but, properly handled, there frequently is sufficient tissue to give one a very good picture of the existing process.

One of the major disadvantages is the large number of patients in which the procedure is contraindicated. It is in those cases where one compromises on the contraindications, in which the complications will arise and discredit may be done to what has proved to be a most valuable procedure. Thus we are very rigid in our criteria about selection of patients and feel it is better not to do it if there is any doubt unless, in weighing the various risks, the information to be obtained is essential for further management of the patient and justifies the risk.

I have here quite a list of what we regard as contraindications. The first includes the "lack of's". For such a simple procedure, a remarkable number of collateral accessories and facilities are necessary if one is going to undertake it safely.

We feel the procedure should be done in the hospital. There should be a capable house staff which is aware of the complications and will recognize the occurrence of any untoward events in the postbiopsy course. There are a few instances in which there have been fatalities following needle biopsy. Most of these in the past have been the direct result of inadequate supervision or management of patients following the biopsy where either they have not been seen at all until they were in a shock-like state, or where, through some error, the patients were not properly supervised or treated. Many of the fatalities thus are direct examples of inadequate postbiopsy care. Needle biopsy should not be performed by one who has not been trained by persons experienced in all aspects of the technic. One obviously should have access quickly to blood for transfusion and an available surgeon. A thorough diagnostic study usually is indicated before undertaking the procedure, the reasons being quite obvious.

Now, as to the "indications for", one should be able to say to himself that the procedure offers at least a reasonable chance of providing information that will influence the management of the patient. An important factor is the ability and will of the patient to cooperate. There also are instances, such as marked ascites, previous surgery on the right thorax or upper abdomen, or anatomical peculiarities where one might not wish to insert a needle blindly. Ascites is not often a factor as it usually can be eliminated.

When the transthoracic approach is used, disease in the right lower lobe of the lung is regarded as a contraindication. Suspected suppurative hepatic disease of the diffuse type may constitute a contraindication.

Another contraindication is possible complete posthepatic obstruction with deep jaundice and potentially great back pressure of bile in the liver. Under these conditions, there is an increased risk of bile peritonitis.

Blood coagulation defects have been ably discussed by Dr. Tocantins so I shall not dwell on them.

What are the conditions in which needle biopsy may be of value? It is quite commonly helpful in the differential diagnosis of otherwise obscure causes of jaundice. There is nothing to be gained by liver biopsy in the ordinary case of acute viral hepatitis if the diagnosis is clear and there are no complications or deviations from the usual course. Biopsy often is indicated to establish the existence of hepatic disease. There are some patients in whom hepatic disease is suspected but in whom other tests may fail to establish its presence or the diagnosis. One may see a patient with existing hepatic disease with known phenomena in the past history that suggests the nature of the present condition.

Yet an entirely unrelated process may be revealed by biopsy as the actual cause. Biopsy also may be of assistance in determining the progress of the disease.

It also may be useful in the diagnosis of certain systemic diseases such as sarcoidosis, tuberculosis, brucellosis, and certain other conditions which elude other specific diagnostic measures.

Liver biopsy has also been of particular value as a research tool. Much of the newer knowledge of hepatic diseases has resulted from the careful use of this procedure in certain selected cases.

We have routinely used the Vim-Silverman needle for this procedure. As you know, there are other technics of liver biopsy including the various aspiration technics.

In a group of approximately 3,500 biopsies* obtained by a similar technic with the Vim-Silverman needle, the incidence of complications is of interest. There have been two deaths in this series yielding the low mortality of 0.06 per cent. The incidence of serious hemorrhage for 2,235 cases was 0.22 per cent, one of these resulting in death.

There was sufficient hemorrhage to require transfusion in 6 cases and operation was required in two cases. Bile peritonitis was reported by only one of the groups occurring after 2 of 620 biopsies.

Dr. Schiff had one patient with what he classified as "non-fatal neurogenic shock". The patient developed a shock-like state not due to hemorrhage but presumed to be due to some reflex of mechanism. We had several instances of a similar reaction, non-serious and non-fatal, which we thought might be due to procaine reactions.

These figures may offer an indication of the risks involved with a standard liver biopsy procedure carried out by experienced personnel.

*Combined series including figures provided by Dr. Leon Schiff and associates for 1,365 biopsies, by Dr. Victor Sborov and associates for 770 biopsies, by Dr. Gerald Klatzkin for 1,440 biopsies, by Dr. Joseph Gambescia for 100 biopsies, and those referable to our own series.

THE PRESENT STATUS OF LIVER FUNCTION TESTS*

S. S. LICHTMAN, M.D.†

New York, N. Y.

It serves a useful purpose to assess medical advances at intervals. Progress, usually slow, is often accepted as a matter of course. In the matter of liver function tests, a note of pessimism is frequently sounded as to their net value in the process of arriving at a diagnosis. There is no definable baseline from which to measure progress. Many may recall the clinical era when the van den Bergh reaction and the icterus index constituted the sum total of liver function tests. There can be little doubt that the current standard tests assist in increasing the accuracy of diagnosis. Needless surgical explorations are less commonly performed. Most patients receive elaborate study in order to increase accuracy in diagnosis.

Technical advances have also been made. The results of liver function tests have been correlated with morphologic changes observed with the assistance of aspiration liver biopsies. The technical advances include bilirubin fractionation employing the photoelectric colorimeter, and more accurate plasma protein fractionation by improved salting out procedures[1-4] and electrophoretic patterns[5-8]. The serodiagnostic tests, although acknowledged to be nonspecific in character and in many respects not liver function tests, have been developed as standard procedures. They supplement the tests for protein metabolism. The BSP retention test, using 5 mg. per kilo and estimation at 45 minutes, has evolved highly dependable and useful.

The attempts to correlate structural and functional changes have proven of limited but definite usefulness[9-12]. A significant, although not close correlation, has been realized. These studies reaffirm and reemphasize the axiom that structural changes are not measurable with any degree of accuracy in terms of abnormal function. This is not surprising since liver fibrosis occurs without significant changes in parenchymal function. The available parenchyma "compensates" for lost functioning tissue. The function tests probe submicroscopic alterations: a "biochemical lesion" may be detected without demonstrable cytological damage. Architectural distortion of liver tissue may occur without disturbance of basic cellular functions. A closer reconciliation between structure and function may eventually be realized if changes in cellular enzymes, cytoplasm and permeability are investigated[13]. This circumstance obviously exonerates the tests as being "insensitive". The correlated studies achieved at least one important point: they postponed indefinitely the prospect of solving the clinical problems

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*Read before the Seventeenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 20, 21, 22 October 1952.

†Assistant Professor of Clinical Medicine, Cornell University Medical College.

of differential diagnosis in jaundice by discovery of a new single liver function test.

Another aspect of the structure-function problem which has been enlightened is the advancement of the concept that, while abnormal structure finds no commensurate counterpart in disturbed physiologic performance, certain hepatic structures are definitely concerned with specific liver functions[14]. The parenchymal cell, the Kupffer cell, the vascular apparatus, and the bile duct system are anatomical units which individually involve special functional capacities.

There would be less difficulty in differential diagnosis if there were a close correlation between the grades of jaundice and the magnitude of histologic change. Unfortunately the opposite is true. Hemolytic jaundice lacks conspicuous hepatic changes. Anicteric cases of viral hepatitis predominate over the icteric. In relapse of jaundice occurring in patients who have recovered from viral hepatitis, the liver biopsy may reveal no significant abnormality[15]. Conversely, jaundice often recedes without coincident regression of pathologic changes. The mechanism for primary intrahepatic obstructive jaundice is still obscure. It frequently becomes established in portal cirrhosis without tangible basis. In the course of infected biliary hepatitis, the tests assume the severity and pattern of diffuse liver damage.

The liver function tests measure patterns of liver damage. The same pattern response is encountered under variable circumstances in intrahepatic disease and in complicated extrahepatic jaundice. An illustrative example of an "abnormal pattern" of liver abnormality is found in metastatic carcinoma of the liver. The BSP test is abnormal in 86 to 100 per cent of cases. On the other hand, in contrast, the flocculation and thymol turbidity reactions are abnormal in only 30 to 40 per cent, respectively[16,17]. Tests of *parenchymal* function frequently remain normal also in massive primary tumors and other focal nontumorous lesions, e.g. echinococcus cyst, follicular lymphomas and sarcoidosis[18]. The metabolic functions remain unaltered, while the tests which reflect circulatory or excretory changes may be impaired. It is a well known fact that infiltrative lesions of the liver such as fatty and amyloid change generally spare parenchymal function. The involvment of nonmetabolic functions is influenced by the extent to which the circulation to the liver and biliary drainage from the liver are interfered with. Now and then, extensive fatty changes occupying the liver cells reduce the amount of functioning cytoplasm with resulting shrinkage of reserve capacity.

The patterns of liver damage are discerned best by application of groups of appropriate tests at the outset of jaundice and then at repeated close intervals as the process subsides or deteriorates. The tests are interpreted in the light of clinical developments. *The skill of the clinical observer outweighs the tests in diagnostic value.* The novice lends too much credence to the tests, the experienced observer cannot do without them. With experience there is increasing probability of correct diagnosis. *The results of the tests, however, overlap too frequently to permit a simple practical formulation for routine use in diagnosis.*

The standard tests recommended for routine clinical use are namely: serum bilirubin fractions, plasma protein fractions, alkaline phosphatase, cholesterol ester partition, prothrombin time, cephalin cholesterol flocculation, thymol turbidity or refinements of the flocculation reactions. Urobilinoids excreted in urine and stool are tested for, mindful of the fact that the oral use of antibiotics may curb the bacterial reduction of bilirubin in the colon. The galactose tolerance test is not performed often enough. Coproporphyrin estimation in the urine and choline esterase determinations in the serum, deserve trial.

Although reference is made to serum bilirubin fractions, current concept leans toward the belief that there is but a single type of serum bilirubin[19,20]. The speed of the diazo reaction depends in great measure on the pigment-protein complex with which it reacts[21]. The renal tubules behave in similar fashion toward the dissociable type of pigment-protein complex: bilirubin is separated and excreted in the urine. *In vitro*, the easily dissociable bilirubin-serum albumin compound reacts readily and rapidly with the diazo reagent: the methylene group of the bilirubin molecule is free to become attached to the diazo reagent. Serum albumin is affixed to the ends of the molecule. Electrophoresis and dialysis studies reveal that diazotized bilirubin migrates with albumin and is not split off in the reaction[22]. Bilirubin forms a stable complex with alpha globulin which behaves differently *in vitro* and *in vivo* from the bilirubin-serum albumin compound. The liver readily splits the former complex apart, for example as in hemolytic icterus. The excess pigment is excreted in the bile. The renal tubule, however, lacks this capacity and the urine is devoid of bilirubin despite an excessive level of serum bilirubin. This suggests that the liver is able to handle the pigment-protein complex through the Kupffer cells which the kidneys lack. *In vitro*, the diazo reaction proceeds differently. A catalyst, such as alcohol or caffein, is required to sever the bond between the methylene group of the bilirubin and alpha globulin before the diazo reaction proceeds. The bilirubin-alpha globulin bond is specific: there is no such complex to our knowledge between bilirubin and the beta and gamma globulins[23].

Normal sera contain minute amounts of alpha globulin and relatively low concentrations of slow diazo-reacting bilirubin. In uncomplicated biliary obstruction there is an excess of regurgitated bilirubin but little increase in alpha globulin. Three moles of bilirubin can combine with one of albumin[23]. Comparative quantitative relationships between bilirubin and alpha globulin are unavailable at present. In retention jaundice associated with liver disease, alpha globulin concentration is likely to be increased, the slow reacting fraction is also elevated. This may also occur in complicated biliary obstruction, accounting for the diagnostic confusion introduced by cholangitis. Increases in the beta and gamma globulin fractions *per se* are not associated with corresponding increases in slow reacting diazo component.

The serodiagnostic tests depend in great measure on the globulin fractions. The cephalin flocculation and cadmium reactions are influenced by alpha globulin.

The thymol turbidity reaction involves the beta globulin fraction in association with a lipid complex. The gamma globulin fraction is tied in with most of the flocculation reactions and more specifically with the zinc sulfate test. In hemolytic jaundice these reactions are all generally negative and there is usually no associated hyperglobulinemia. It is common knowledge that these tests when positive do not necessarily implicate hepatic disease. Reticuloendothelial disorders are associated with hyperglobulinemia and positive flocculation tests. When the liver itself is not actively involved, the standard liver function tests remain negative. Hyperglobulinemia is not always associated with positive flocculation reactions. For example, in multiple myeloma they remain negative.

The cholesterol and phosphatase determinations are somehow bound up in the phase of recovery, regeneration and/or immunity. Hypercholesterolemia and increased serum alkaline phosphatase are interpreted as signifying cellular overactivity or regeneration of certain liver tissue under special circumstances. These substances accumulate in the blood beyond the range of biliary excretion; the kidneys are unable to drain off either substance. The reverse, a decline in cholesterol and its ester fraction and a low level of serum alkaline phosphatase attended by jaundice, is an expression of liver cell underactivity. The presence of low cholesterol ester values is significant evidence of severe liver damage. Other tests generally confirm this fact. When it is an isolated finding and other liver function tests remain normal, it suggests mechanical obstruction with secondary liver impairment[24].

Jaundice is the major clinical expression of hepatobiliary disorders. Accordingly every effort has been devoted to devising measures for differentiating the types of icterus. Hemolytic and nonhemolytic types of jaundice can positively be differentiated by the bilirubin pigment tests and ancilary hematological studies. Retention and regurgitation types of jaundice marked by obstructive features cannot, however, be differentiated by the pigment tests *per se*. The same applies to the BSP retention test, the dye analogue of bilirubin: when this test is applied in cases of jaundice with obstructive features of hepatic or posthepatic types, it is worthless in differential diagnosis.

The tests which do assist in differentiating medical and surgical jaundice are those which are concerned with parenchymal damage. These include the cholesterol partition, alkaline phosphatase, the plasma protein fractions and the serodiagnostic tests based on them. It is worthy of comment that the BSP test assists materially in the diagnosis of liver damage especially when jaundice is inconspicuous. A marked grade of BSP retention under these circumstances is highly suggestive of marked liver damage or circulatory impairment. Prolonged and complicated biliary obstruction introduces disturbing elements in diagnosis. Under these circumstances, the observation and interpretation of clinical events are indispensable adjuncts and decisive in the final analysis. The tests are no substitute for clinical skill.

The liver function tests are as indispensable for adequate management of patients with hepatobiliary disease as they are for diagnosis. This adds considerably to the cost of treatment since the tests require skilled technicians and fully equipped laboratories. There can be no compromise on this score. Simple tests which truly do not measure liver function cannot supplant reliable, accurate and complicated technical procedures, for economic and technical expediency. *The icterus index cannot replace the determination of the bilirubin fractions.* It is our opinion that the icterus index has no further place as a test of liver function in a modern hospital or laboratory. The flocculation and turbidity tests cannot be employed in place of the serum protein fraction determinations. The flocculation and turbidity reactions are being used *incorrectly* as the *sole* laboratory guide by some in the diagnosis and management of patients with liver disease partly because of lack of adequate facilities, and partly because these tests can be performed routinely and economically in large numbers with limited technical assistance.

The liver function tests also play an indispensable role in screening industrial applicants, blood donors for subclinical liver disease, and in evaluating the toxicity of pharmaceutical agents before clinical release.

Summary

There has been a gradual and progressive advance in the use of liver function tests for diagnostic and screening purposes. Reliable and accurate technics have been evolved. The problem is simplified if it is recognized that the tests measure patterns of liver disease, not specific disorders. This requires the use of several tests repeated at frequent intervals. There is only a superficial agreement between the results of the tests and structural changes as judged by routine histopathologic technics. This discrepancy does not discredit the value of the tests as being insensitive. With limitations recognized, emphasis is placed on learning the "patterns of abnormality". Integrated with significant clinical facts and events, the tests are indispensable adjuncts to correct diagnosis and management of patients with hepatobiliary disease. The serial determination of the selected group of tests adds greatly to the cost of diagnosis and treatment. There can be no compromise by substitution of scientifically unreliable and inaccurate procedures for testing liver function on the grounds of economic or technical expediency.

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HISTOLOGIC CRITERIA FOR THE DIFFERENTIAL DIAGNOSIS OF LIVER DISEASES IN NEEDLE BIOPSIES*†

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The varied terminology and nomenclature of liver disease, in both clinical and pathologic fields, have led and still lead to considerable confusion. With clearer histologic definition of the basic pathologic entities it is hoped that a simple and more uniform terminology will evolve. The need for this has become more urgent as a result of the increased popularity of needle biopsy of the liver as a diagnostic procedure. In the interest of better understanding it seemed desirable to record the terms and diagnoses used by the Registry of Hepatic Pathology, Armed Forces Institute of Pathology, together with the histologic criteria for the various pathologic entities which are encountered more frequently in the material submitted.

Since it is but rarely possible to make a specific etiologic diagnosis, the Registry supplies a descriptive diagnosis which, at least, narrows down the possibilities to a limited number of etiologic factors. This "group diagnosis" serves to exclude other broad categories of disease processes.

A list of the diagnoses currently used in the Registry of Hepatic Pathology follows and the histologic criteria for each are briefly described.

1. Normal, or minimal histologic changes
2. Fatty metamorphosis
3. Passive congestion
4. Paracentral necrosis (anoxic)
5. Central necrosis, etiology undetermined
6. Focal necrosis, etiology undetermined
7. Toxic hepatitis (specify agent if known)
8. Portal cirrhosis
9. Cirrhosis, type undetermined
10. Portal fibrosis, etiology undetermined

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11. Bile stasis, obstructive type (obstructive jaundice)
12. Cholangitis and pericholangitis
13. Biliary cirrhosis
14. Hemosiderosis
15. Hemochromatosis
16. Viral hepatitis
    a. Active hepatitis
    b. Subsiding hepatitis
    c. Persistent hepatitis
    d. Postnecrotic collapse and postnecrotic scarring
    e. Coarsely nodular cirrhosis (postnecrotic cirrhosis)
17. Infectious mononucleosis
18. Granulomas or granulomatous hepatitis
19. Specific infectious disease process, with the etiologic agent demonstrated
20. Hamartia and hamartomas
21. Primary neoplasms
    a. Benign epithelial
    b. Benign mesenchymal
    c. Malignant epithelial
    d. Malignant mesenchymal
22. Secondary neoplasms
23. Effects of operative trauma (surgical biopsy); subcapsular scarring
24. Miscellaneous

1. *Normal Liver or Liver Showing Minimal Histologic Changes:*—In some specimens the histologic changes are minimal and nonspecific so that no categorical diagnosis can be made. In order to determine whether such minimal changes can be correlated with any clinical or biochemical features, the Registry of Hepatic Pathology is at present segregating cases with minimal histologic changes from those that appear entirely normal. For the latter group the term "within normal limits" is used, and for the former, "minimal histologic changes, etiology undetermined". The cases that generally fall into the latter category are those that show (1) an unusual degree of pleomorphism of parenchymal cells without other significant cytologic alterations, (2) a minimal degree of inflammation in the portal areas or in the lobules, and (3) occasional focal necrosis. These minimal histologic changes are probably of no significance in the over-all function of the liver, but this problem awaits further study.

2. *Fatty Metamorphosis (specify degree):*—Fatty metamorphosis, unless it occurs in conjunction with portal cirrhosis or toxic hepatitis, is recorded separately. While ordinarily only an occasional liver cell contains cystoplasmic fat, there are conditions in which fat droplets, varying in size and number, can be demonstrated in many of the hepatic cells. The entire cytoplasm may be replaced by fat which pushes the nucleus aside in signet-ring fashion. The transformation is sometimes so marked as to make histologic recognition of the organ difficult

were it not for the portal triads. Fatty metamorphosis may be the sole change, without parenchymal necrosis, portal fibrosis or inflammation. It is not known whether in different cases of fatty metamorphosis the fat is of identical biochemical nature and whether it always is an expression of dysfunction of liver cells secondary to injury.

In some instances fatty metamorphosis is associated with small foci of necrosis of liver cells surrounded by small clusters of inflammatory cells. Occasionally definite Mallory bodies, similar to those found in portal cirrhosis, are seen. The fatty metamorphosis and focal necrosis may be accompanied by varying degrees of portal fibrosis and inflammation. Since it is not clearly established that such a picture is necessarily the precursor of portal cirrhosis, the term "early cirrhosis" is used in this connection only speculatively.

3. *Passive Congestion:*—In passive congestion the sinusoids become more prominent because they are stuffed with blood. This congestion becomes more pronounced as one proceeds from the portal canal toward the central vein. In chronic cases the congestion is accompanied by atrophy of the liver cells which is more pronounced toward the efferent vein, so that the liver cords appear to taper; the cells at the periphery of the lobules are fairly intact while those near the central vein are obviously smaller. This process apparently takes place gradually, because in acute passive congestion tapering of the liver cords is absent.

Actual cases of cardiac cirrhosis are extremely uncommon. In very rare instances the congestion of the sinusoids is due to primary disease of the hepatic veins and their branches, with thrombosis of some of the intrahepatic radicals (central cirrhosis of Chiari).

4. *Paracentral Necrosis (Anoxic):*——The form of hepatic necrosis seen in anoxic conditions is highly characteristic. The localization of the areas of necrosis is usually somewhat off center, occurring just to one side or other of the central vein. The lesion represents a coagulation type of necrosis of liver cells associated with a varying number of polymorphonuclear leucocytes, at times so numerous as to cause it to resemble microabscesses. The earlier phase of this anoxic form of necrosis consists of a peculiar cytoplasmic vacuolization of the individual liver cells, the vacuoles containiag neither fat nor glycogen but fibrinoid inclusions. The lesion may be seen following hypoxia or anoxia from various causes, such as high altitude, circulatory collapse following hemorrhage or shock, and pneumonia.

5. *Central Necrosis:*—The term, "central necrosis, etiology undetermined", is used if the origin of the necrosis is not clear. Sometimes there is slight centrolobular fibrosis accompanied by macrophages containing lipochrome pigment. It has been suggested that central fibrosis associated with pigment may represent the residues of a previous attack of toxic hepatitis or anoxic necrosis.

6. *Focal Necrosis, Etiology Undetermined:*—This term is used for cases in with the foci of necrosis of liver cells are haphazardly scattered throughout the

liver lobules without any particular zonal distribution. These foci are generally surrounded by small numbers of inflammatory cells of mononuclear character and there may be slight degrees of diffuse intralobular inflammation and portal infiltrates. (For other types of focal necrosis refer to paragraph 19 in which specific disease processes are discussed).

7. *Toxic Hepatitis:*—There are several histologic varieties of toxic hepatitis, depending upon the toxin or poison involved. Distinct entities are those produced by the halogenated hydrocarbons, such as carbon tetrachloride or chloroform. In carbon tetrachloride poisoning there is aseptic acute necrosis of the centrolobular portions of the liver accompanied by congestion. The central regions are seen as sharply punched-out areas of necrosis, within which are small numbers of inflammatory cells and Kupffer cells loaded with lipochrome pigment. These Kupffer cells are generally restricted in the central areas of necrosis, in contrast to their diffuse distribution in viral hepatitis. Since Kupffer cells ordinarily do not contain lipochrome, it is assumed that this pigment is phagocytized from necrotic liver cells. The early phase of chloroform poisoning is characterized by fatty metamorphosis, particularly of the central portion of the lobule, while the later stages closely resemble those seen in carbon tetrachloride intoxication.

The presence and location of pigmented Kupffer cells is of considerable aid in determining the site of the previous liver damage, particularly after healing or regeneration has supervened. For example, in needle biopsy specimens taken after clinical recovery from carbon tetrachloride poisoning, pigmented Kupffer cells in centrolobular areas were the only residues of the previous damage.

Other poisons may produce an entirely different picture. For example, in arsenic or phosphorus poisoning there may be only mild fatty metamorphosis and minimal necrosis, generally restricted to the centrolobular areas but occasionally found in other zones. The effects of mushroom poisoning on the liver may simulate those of acute fatal viral hepatitis or of phosphorus poisoning. There are many newly introduced chemical solvents and substances whose possible actions on the liver parenchyma are still uncharted.

In most instances toxic hepatitis is characterized by necrosis of liver cells accompanied by minimal inflammation and varying degrees of fatty metamorphosis.

8. *Portal Cirrhosis (atrophic cirrhosis, Laennec's cirrhosis, monolobular cirrhosis, etc.):*—In the Hepatic Pathology Registry the term "cirrhosis" is not employed as a synonym for simple portal fibrosis but indicates a completely altered hepatic architecture characterized by varying degrees of pseudolobulation.

In the fully developed portal cirrhosis the entire liver is transformed into a micronodular organ comprised of numerous small pseudolobules. Portal cirrhosis is considered to be a diffuse hepatic disease which involves practically all of

the parenchyma and portal canals in a fairly uniform manner. Numerous small bile ducts and an increased amount of collagenous tissue are seen in portal areas and in the periphery of the pseudolobules. The central veins in all pseudolobules are abnormally located and often lie close to the portal canals; sometimes efferent veins cannot be demonstrated in many lobules. In the later stages there may be larger areas of hepatic destruction in which only scar tissue and small bile ducts remain. In the over-all picture, however, these changes are not prominent and should not be mistaken for a postnecrotic or coarsely lobular cirrhosis.

Portal cirrhosis may or may not be associated with varying degrees of fatty metamorphosis. In general, it may be stated that fatty metamorphosis, for all practical purposes, has been seen more commonly in cases of cirrhosis of the portal type and, when present, is of considerable assistance in arriving at that diagnosis.

The term "cirrhosis" has a definite functional connotation, since the abnormal architecture causes serious disturbances in vascular supply and function of the liver. The cirrhosis, once established, sets in motion a series of events which are the sequelae of the disturbed architecture of the liver and which may be quite separate from the damage produced by the original irritant. An analogy might be the functional sequelae of mitral stenosis itself, quite apart from cardiac disturbances produced by the acute phase of rheumatic fever.

The exact histogenesis of portal cirrhosis is as yet unknown. It may perhaps be assumed that definite pseudolobulation may be absent in the earlier stages of portal cirrhosis; however, a rather characteristic picture which is seen at times may perhaps represent a stage in the development of cirrhosis of the portal type. It includes necrosis of liver cells, portal and intralobular fibrosis, and inflammatory infiltrates of both portal canals and parenchyma, with or without fatty metamorphosis. The necrosis involves liver cells singly or in groups, diffusely and irregularly scattered through the lobules. Many of the affected cells present a well preserved nucleus but partial or complete transformation of the cytoplasm into coarse intracytoplasmic hyaline masses, commonly referred to as Mallory bodies. A considerable amount of inflammatory reaction is generally scattered throughout the lobules, particularly adjacent to necrotic liver cells and the cells containing Mallory bodies. Special stains indicate that collagen is usually increased in amount in the portal canals and occurs in the form of thin bands traversing the affected parenchyma of the lobules. These bands disrupt the normal lobular structure and perhaps form the basis for the final architectural abnormality, since the parenchymal regeneration which follows may be forced into an aberrant pattern by the haphazard arrangement of the new hepatic framework. This reorganization is associated with the formation of portocaval shunts which may specifically alter the function of the liver, while the abnormalities in the vascular pattern due to the reorganization of the lobules lead to portal obstruction and its consequences.

9. *Cirrhosis, Type Undetermined:*—Cases which show pseudolobule formation but do not fulfill the criteria for cirrhosis of any of the types already outlined or still to be described are designated as cirrhosis, type undetermined. Some of the cases of cirrhosis associated with Wilson's disease probably belong in this group because of the peculiar nodular hyperplasia of regenerated liver lobules and the rather delicate septa between well preserved parts of the parenchyma.

10. *Portal Fibrosis, Etiology Undetermined:*—This term is used for cases in which the amount of portal collagenous tissue is definitely increased, sometimes with the added features of real or apparent increase in the number of small bile ducts and the presence of varying numbers of mononuclear cells and eosinophils. Pseudolobulation, however, is absent. The etiology, histogenesis and pathogenesis usually remain obscure. In cases where changes of this type are clearly related to a previous attack of viral hepatitis, the term "postnecrotic scarring" or "postnecrotic collapse" is used. Comparable lesions have also been observed in the wake of granulomatous hepatitis.

11. *Bile Stasis, Obstructive Type (Obstructive Jaundice):*—In the jaundice resulting from obstruction of the main bile ducts the early changes are confined to the centrolobular zones and consist of bile thrombi in bile canaliculi with extensions into liver cells. In cases uncomplicated by infection the portal canals and lobules are usually free of inflammatory reaction; in others the biliary obstruction may be complicated by cholangitis or pericholangitis.

The restriction of the bile retention to the bile canaliculi in the central portion of the lobules reflects the consequences of exertion of the greatest pressure on the most delicate and weakest structures of the biliary system.

12. *Cholangitis and Pericholangitis:*—The term cholangitis is restricted to those cases in which inflammatory cells, generally polymorphonuclear leucocytes, are actually found within the lumina of the bile ducts. If the lumina are free of inflammatory exudate and infiltrates consisting of polymorphonuclear leucocytes are found only immediately adjacent to the bile ducts of the portal triads, the term pericholangitis is employed. It seems important to differentiate between these two entities since a different mode of spread is implied. In cholangitis the inflammatory process probably spreads by direct extension along the lumina of the ducts, whereas in pericholangitis the spread is probably either by lymph or blood. In cases of cholangitis or pericholangitis the inflammation may be restricted to the portal areas; in some instances, however, the inflammatory process spreads to the lobules. A varying degree of obstructive bile stasis is usually observed in the centrolobular zones; when this occurs in conjunction with pericholangitis it is difficult, on histologic grounds alone, to determine whether the obstruction is of the extrahepatic or intrahepatic variety. In some cases the data suggest that there may be a primary inflammation of the intrahepatic biliary system with resultant bile stasis, but in most instances the evidence is not clear enough to warrant a definite statement.

The terms "cholangiolitis", "cholangiolitic hepatitis" and "cholangiolitic cirrhosis" are not used in the Registry of Hepatic Pathology, since no clear and uniform histologic counterparts have been found for the clinical entities that bear these names. Intralobular "cholangioles" have ordinarily not been seen in either normal or pathologic liver specimens. The small bile ducts seen in lobules in a few cases have been interpreted as preformed structures, probably hamartias. Some cases bearing these clinical diagnoses have presented histologic evidence of pericholangitis and bile stasis, which adequately explain the clinical and laboratory findings.

13. *Biliary Cirrhosis:*—This form of cirrhosis comes about as a result of a long-standing alteration of the biliary passages obstructing the flow of bile. It can be produced by malformation or inflammation of biliary passages or by pressure on the intrahepatic or extrahepatic bile ducts due to inflammatory processes of neoplasms.

In this condition the portal triads are larger than normal and the amount of portal collagenous tissue and the number of small bile ducts are increased. Later, definite pseudolobulation may occur. In the active phase bile stasis is always present; in the earlier stages this is confined to the bile canaliculi of the centrolobular regions, but bile lakes, phagocytosis of the bile by Kupffer cells, and cellular damage by bile extravasates may soon become apparent. Unfortunately the term "biliary cirrhosis" has been used traditionally even when definite pseudolobulation has not yet occurred. It is suggested that the term be reserved for cases in which pseudolobulation has developed, and that the earlier stages of this process be designated as a preliminary condition, such as cholangitis or pericholangitis, with or without portal fibrosis, or as obstructive bile stasis, naming the cause.

14. "*Hemosiderosis*" is used for cases in which the amount of hemosiderin in Kupffer cells, parenchymal cells, or both, is excessive. This may be the result of blood transfusions or various exogenous or endogenous factors. Cirrhosis is not a necessary consequence of hemosiderosis but may be present incidentally.

15. *Hemochromatosis:*—The term "hemochromatosis" is used to characterize portal cirrhosis with deposition of hemosiderin pigment in liver cells, Kupffer cells, epithelium of bile ducts, and phagocytic cells of the stroma. We restrict its use to those cases of pigmented cirrhosis associated with hemosiderosis of the skin or diabetes mellitus, preferably both. Since iron is retained in occasional cases of portal cirrhosis, giving the picture of portal cirrhosis with hemosiderosis, it is difficult on the basis of the biopsy specimen alone to differentiate between portal cirrhosis with hemosiderosis and true hemochromatosis.

16. *Viral Hepatitis:*—(Infectious hepatitis, epidemic hepatitis, homologous serum hepatitis, transfusion hepatitis, etc.) The histologic picture of the nonfatal form of viral hepatitis is characteristic in the acute phase but becomes increasing-

ly nonspecific as the disease runs its course. For this reason, this condition will be discussed under the headings of acute, subsiding, and persistent viral hepatitis.

a. In the *acute phase* the histologic appearance is highly specific and the needle biopsy is the only single laboratory procedure which permits definitive diagnosis. The term "active hepatitis" is used to refer to the acute phase of this disease. Biopsies performed immediately after the onset of clinical jaundice reveal necrosis involving single cells or small groups of liver cells throughout the lobules, accompanied by a prominent portal and lobular inflammatory reaction consisting predominantly of mononuclear cells and small numbers of eosinophilic leucocytes. Polymorphonuclear leucocytes are sparse except in rare cases where pericholangitis appears to be a complication. This combination of necrosis and inflammation results in a disturbance of the normal architecture of the lobule; the cohesiveness of the liver cells is lost and the cells appear to have fallen away from each other.

A peculiar form of degenerated liver cell, termed the "acidophilic cell", is frequently seen in viral hepatitis. This cell is characterized by a small dark pyknotic nucleus and a hyaline, homogeneous, acidophilic cytoplasm. It can generally be differentiated from the Councilman body of yellow fever because of its homogeneity and from the partial cytoplasmic necrosis characteristic of the Mallory body. While such cells are fairly numerous in viral hepatitis, they are not pathognomonic for this disease since they also occur in other conditions, although rarely as prominently as in viral hepatitis; such conditions are: necrosis of liver cells following tannic acid treatment of burns, poisoning by a variety of toxic agents, longstanding bile stasis, rapidly advancing cirrhosis of the liver, and others.

Concomitant with necrosis is a process of active regeneration. Many pleomorphic liver cells are seen, some with two or more nuclei containing prominent nucleoli; mitoses are common. The over-all picture is variegated and at times the combination of necrosis, inflammation, and regeneration results in a bizarre appearance. The Kupffer cells are prominent and many contain a finely granular pigment, consisting chiefly of lipochrome liberated from necrotic parenchymal cells. Varying amounts of hemosiderin may also be present in Kupffer cells or may be entirely absent. The presence of hemosiderin pigment suggests either a disturbance in the iron metabolism of the liver or a liberation of ferritin. In either event the diffuse distribution of pigmented Kupffer cells throughout the lobules is indeed a reflection of the generalized distribution of parenchymal damage.

Although there is clinical jaundice in most of the acute cases, bile retention is seldom prominent in the early stages. The clinical icterus may be due to disruption of the delicate bile canaliculi, permitting bile to flow into the sinusoids.

b. The *subsiding phase of viral hepatitis*, which occurs generally three or four weeks after the onset of clinical jaundice, is also fairly characteristic. The

portal infiltrates are still prominent. The inflammatory reaction in the lobules has become less diffuse and tends to focalize, especially about individual necrotic liver cells. Regeneration of parenchymal cells has progressed to a remarkable degree and some of the bile canaliculi may show bile thrombi, possibly the result of temporary obstruction of these canaliculi by regenerating liver cells. The iron pigment, which earlier is distributed irregularly, slowly migrates toward the portal areas. The lipochrome pigment in the Kupffer cells appears to persist for a period of from two to three months. Some collapse of the periphery of the lobules may be seen, and a study of preparations stained with reticulum and Masson stains indicates that the widened portal areas are, in all probability, the result of condensation of reticulum fibres, perhaps exaggerated by inflammatory edema. At this stage the term "postnecrotic collapse" would seem more appropriate than "postnecrotic scarring". Apparently the last changes to disappear (in the usual case of hepatitis which goes on to healing) are the portal infiltrates and the pigment in Kupffer cells.

c. *Persistent Viral Hepatitis:*—Generally at the end of three months, restoration is complete and only minimal portal infiltrates remain. In certain cases, however, which have been followed by serial biopsies, the inflammatory process has persisted for several months. In these instances the portal areas and the lobules still contain inflammatory cells, although the process in the lobules tends to be focal rather than diffuse. Necrotic and acidophilic cells may still be seen, but less lipochrome pigment is found in Kupffer cells. Such cases are interpreted as representing the effect of prolonged viral infection and are designated "persistent viral hepatitis".

Although there is no difficulty in distinguishing pericholangitis from viral hepatitis in the acute phase, some cases of chronic pericholangitis may be difficult to separate from persistent viral hepatitis.

d. Definite pathologic criteria characteristic of "chronic viral hepatitis" have not yet been established. With time the picture becomes progressively less specific. Certain features in long-standing cases, however, merit attention. When the disease has lasted from six to twenty-four months, for example, it has been noted that the changes become less diffuse and more irregularly scattered. Certain lobules may be entirely free of histologic change while the normal structures of others may be replaced by large areas of scarring in which numerous mononuclear cells are seen. The distribution of portal fibrosis and inflammation is irregular and haphazard. Inflammation in the lobules becomes less and less common and may be represented only by small foci of necrosis of liver cells and small clusters of mononuclear cells. The postnecrotic condensation of reticulum fibres at the periphery of the lobules seems to give way gradually to collagen. In cases where the portal fibrosis is definitely associated with a previous attack of acute viral hepatitis the term "postnecrotic scarring" seems appropriate. It is believed that a distinction should be made between the "postnecrotic collapse"

of the acute phase and the "postnecrotic scarring" in some of the more persistent cases.

The gradually changing reaction of the liver tissues to the virus is attributed to the attainment of a state of equilibrium between the virus and the organ, comparable to that observed with the herpes virus.

e. Coarsely lobular cirrhosis (coarsely nodular cirrhosis, or postnecrotic cirrhosis) is tentatively placed in this category although its etiology and pathogenesis are not clearly related to viral hepatitis. Many students in this field, however, believe that should cirrhosis develop as a consequence of viral hepatitis, it would probably be of this type.

In contrast to the micronodular form seen in the portal type of cirrhosis, coarsely nodular cirrhosis is characterized by the development of larger nodules surrounded by thin or thick bands of scar tissue. These larger nodules may enclose several lobules in which both the parenchyma and the portal canals are often normal. There may be extensive, broad areas of scarring containing increased numbers of bile ducts and varying amounts of inflammatory cells. In the more normal lobules enclosed within the larger coarser nodules, the central veins usually stand in normal position. Because of the variations within such a liver, it is often difficult in biopsy material to distinguish between the coarsely nodular and the portal type of cirrhosis. If, however, one or more central veins can be found in normal position, the possibility of a postnecrotic form of cirrhosis should be given due consideration. Whether the large lobules represent surviving liver tissue or orderly regeneration following a single severe injury remains undetermined.

17. *Infectious Mononucleosis:*—The only histologic picture which may be confused in biopsy material with acute viral hepatitis is that of infectious mononucleosis. There are, however, several minor differential points which are worthy of note. The portal infiltrates in infectious mononucleosis generally consist of large numbers of mononuclear cells. Cells of the same type infiltrate the sinusoids in a creeping fashion, producing little, if any, disruption of the lobular architecture. The severe inflammatory reaction is out of proportion to the minimal degree of necrosis. In repeat biopsies there appears to be little change in the appearance of the liver during the course of the disease.

18. *Granulomas or Granulomatous Hepatitis:*—This entity is characterized by well defined granulomas usually composed of epithelioid cells and giant cells of the Langhans type. In some cases these granulomas tend to localize predominantly in the portal areas, while in others their distribution is random through the lobules. Where etiologic agents, such as acid-fast bacilli, spirochetes, histoplasma, fungi, ova of parasites, etc., can be demonstrated they should be specified; otherwise the case is designated as "granuloma, etiology undetermined".

In some cases the granulomas are accompanied by a diffuse intralobular inflammation. Indeed, in some instances the presence of a nonspecific diffuse hepatitis has led to further study, with the result that underlying granulomas have been found in deeper sections. If healing takes place, the portal canals usually show an increase in fibrous connective tissue. On rare occasions this change is generalized and imitates cirrhosis, but usually it results in portal fibrosis, the etiology of which is obscure if the granulomas have disappeared.

19. *Specific Disease Processes with the Etiologic Agent Demonstrated:*—Examples are amebiasis (with abscesses containing organisms), granulomas due to schistosomiasis, tuberculosis, fungus diseases and leprosy, as well as focal necroses of typhoid fever. Yellow fever produces characteristic midzonal necrosis and Councilman bodies in the liver and may be included in this group.

20. *Hamartias* and *Hamartomas* are not uncommon and are represented by cavernous hemangioma or by bile duct "adenoma".

21. *Primary Neoplasms:*—Where there is clear-cut evidence of a primary neoplasm of the liver the diagnosis is made accordingly. The benign neoplasms include (a) epithelial (e.g. adenoma) and (b) mesenchymal tumors (e.g. fibroma, angioma). Primary malignant epithelial neoplasms (c) are represented most frequently by the liver cell carcinoma (hepatoma) or the primary bile duct carcinoma (cholangioma). Primary malignant tumors of mesenchymal origin (d), such as hemangioendothelioma or various types of sarcomas, may also be found in the liver.

22. *Secondary Neoplasms:*—In the case of metastatic tumors in the liver, it may be difficult to determine the primary site of the neoplasm from a biopsy specimen. In such instances, the term "malignant neoplasm, primary site undetermined" is generally used. Sometimes, however, the type of cell (oat cell, signet-ring cell, columnar cell, vacuolated cell), presence of pigment (melanoma), or the architecture of cell groups (papillary structures) suggests the place of origin of the original neoplasm.

23. *Effects of Operative Trauma (Surgical biopsy):*—Surgical specimens of liver taken during laparotomy frequently show the effects of operative trauma, particularly if removed toward the end of a lengthy operation. Fresh hemorrhage, necrosis, and infiltration by polymorphonuclear leucocytes are the usual changes induced.

The surface of the liver is often the site of scarring which is absent in the deeper portions of the liver. In many instances it is difficult to differentiate between this "subcapsular scarring" and a true cirrhosis. Conversely, in true cases of portal cirrhosis the superficial parts of the liver may fail to show the characteristic micronodular pseudolobulation which is present in the underlying tissue. The changes resulting from exposure and manipulation of the liver during surgical procedures and the misleading nature of surface abnormalities consti-

tute strong arguments for the needle biopsy. Although less tissue is removed with the biopsy needle the specimen so obtained constitutes a more representative sample; moreover, the method lends itself to follow-up study.

24. *Miscellaneous:*—This group comprises various pathologic entities which are found only occasionally and incidentally. Examples are amyloidosis, Gaucher's disease, von Gierke's disease, polycystic disease, congenital malformation of intrahepatic bile ducts, cirrhosis of the liver in Wilson's disease, hematin pigment in Kupffer cells in cases of malaria and schistosomiasis, thorotrast pigment in liver, and various other conditions.

Comment

The need for improved methods of diagnostic and investigative procedure in the field of liver diseases has recently led to an increasing use of the needle biopsy of the liver. Many clinical conditions can be diagnosed only by performing a liver biopsy. Despite the small amount of tissue obtained with this method, the needle biopsy specimen is considered superior to the wedge surgically removed, because in the former artefacts are avoided and a deeper, more representative sample is obtained; in addition, the method lends itself to follow-up studies. The small size of the specimen, however, makes it mandatory that the pathologist have an intimate knowledge of all the pathologic details that can be observed in a needle biopsy specimen. When this knowledge has been mastered and the specific criteria of the many disease processes have been sorted out, an accurate pathologic diagnosis can be made in the great majority of cases.

Discussion

Dr. Joseph Post (New York, N. Y.):—You have heard a great deal of information this morning and I shall not attempt to discuss in detail any of the papers. There are a few points I want to bring up and they are in areas where I have had some personal experience.

First of all, there is the question of the relationship of structure to function. I am afraid it is something that will plague us for many, many years until we learn more about function.

Dr. Lichtman has indicated that many of our tests do not measure liver function as such, albeit they are very valuable in the detection of liver disease. In the studies we made three or four years ago in Laennec's cirrhosis, we felt that the histological appearance of the liver could not be correlated with either the function tests as ordinarily measured, or the clinical state of the patient. We could find some correlation between the clinical status of the patients and the level of serum albumin, but in attempting to define the histopathologic changes as seen by routine technics, we were unable to come up with any kind of correlation. That is not remarkable, really, when we stop to think about it a moment.

When we examine a relatively simple test like the cephalin flocculation and try to relate it to any cytological change, it becomes extremely complex. We know very little about the basic biochemical factors involved in elaboration of albumin in the liver cell, let us say, or the basic influence of liver cell metabolism on the globulin fractions or upon the lipid fractions in the blood. All of these biochemical entities are involved in the cephalin flocculation. It is perhaps a bit of mistaken oversimplification to correlate structural changes with function tests in the light of our limited knowledge.

It is a treat for me to hear Dr. Smetana talk about his systemization of diagnosis of biopsy material because many of us for years have had trouble in interesting pathologists in these biopsies. Many people in the field are beginning to feel that biopsy portrays the liver in as close to its natural state as any technic we have had up to today.

I want to ask Dr. Smetana whether he thinks that the process of periportal fibrosis which he described is at all related to the genesis of Laennec's cirrhosis. We are at present very much interested, in our laboratory, with this histological change.

We feel that in general the liver biopsy is another very valuable and useful technic being taken along with the laboratory tests of so-called liver function, and the appearance of the patient. Any one of these things by itself, considered alone, is going to lead us to make more mistakes. All three together, I think, increase the accuracy of diagnosis tremendously.

I wanted to show you some kodachromes of biopsies that we have, demonstrating some of the cytochemical technics that can be applied to the biopsy, but, unfortunately, the kodachrome projector is not here.

Let me say that a variety of problems are under investigation today, many of which are made possible solely because we are now able to obtain a piece of liver tissue on a contemporary basis rather than being dependent upon the occasional, rare operative biopsy. The operative biopsy carries with it a great many artefacts which we do not understand. The biopsy specimen provides a piece of tissue that can be studied by a variety of methods, by routine histologic stain, by more specialized stains for the distribution of glycogen, alkaline phosphatase, and desoxyubosenucleic acid. There are many basic problems which can be studied, which until now were inaccessible because we had to depend on the autolyzed piece of tissue obtained at postmortem table.

In addition some groups are now starting to study the liver cell with the electron microscope, a technic which heretofore could never be adapted to the liver.

Dr. I. R. Jankelson (Boston, Mass.):—I believe I express the general opinion when I say that this was a very productive morning, with extremely interesting

papers, and very instructive material. I know all of us are grateful to the essayists who presented these papers.

I should like to limit my discussion to Dr. Neefe's paper. I think Dr. Neefe has well presented his method of liver biopsy, and its advantages and I need not say anything more about it. For approximately a year a group of us at Boston City Hospital, including Dr. Baker, Dr. Zamchek, and myself, have tried to correlate liver biopsy in cirrhosis of the liver with a pattern of visible abdominal veins as demonstrated by infrared photographs. We have now approximately 30 cases of liver cirrhosis, all proven by liver biopsy.

The correlation apparently is very good in so far as the greater the increase of fibrosis in the liver the more marked is the pattern of veins of the abdominal wall.

I want to present three slides as representative ones.

(Slide) This is an infrared photograph of a normal young woman who had no evidence of liver disease. There are practically no veins demonstrable in this case.

(Slide) This is a case of virus hepatitis, which, too, shows just a few minor veins of no significance.

(Slide) This third slide shows an advanced case of cirrhosis of the liver, which demonstrates the markedly enlarged veins of the abdominal wall. We don't get such beautiful pictures in every case, but even in moderate cases we begin to see a pattern of demonstrable veins by infrared photography.

There is another corollary which I might mention now. In our experience so far, we believe these demonstrable veins by infrared photography appear before enlargement of the veins of the esophagus as seen by esophagoscopy or x-rays. As such we think it is a worthwhile screening process in the demonstration of cirrhosis as the cause of upper digestive tract hemorrhage, which may otherwise remain unexplained.

Dr. N. B. Jaffe (*Bridgeport, Conn.*):—My question is not intended for any particular gentleman who spoke, but I should like to know what is the present status of gallbladder drainage or duodenal intubation in the diagnosis of liver disease.

Dr. Hyman I. Goldstein (*Camden, N. J.*):—This was indeed, an intellectual treat.

The presentations today were eloquently and informatively presented. During the past twenty years I know of no meeting and no symposium that exceeded or even equalled the presentations by the experts we heard this morning. The audience should realize that they have heard today from one of the leading hematologists in the country, Dr. Tocantins; one of the leading exponents in

the Philadelphia area, of liver studies and liver biopsy, Dr. Neefe; Dr. Lichtman, who recently issued a splendid new edition of his encyclopedic work on the liver, and from Dr. Post, who did pioneer work in the therapy of these diseases. We have heard diagnostic problems, but Post and others have really revived the newer therapy for these diseases; and, briefly, we heard from Smetana, too, and we heard about "Mallory bodies", and the "Councilman bodies". We did not (inadvertently) hear of the "Masson bodies" in carcinoid disease, and the "*Kulchitsky cells*"!

It is just about twenty years ago that W. Morrell Roberts first definitely reported in a series of cases, two clinical cases in which he, for the first time in medical literature, specifically observed the pronounced—and I quote, "the pronounced"—elevation of the alkaline phosphatase in obstructive jaundice as a diagnostic criteria, and one case was in conjunction with Hodgkin's disease of the liver which is interesting. Roberts made interesting observations on the nature of the van den Bergh Reaction and he studied blood phosphatase activity in obstructive jaundice and osteitis deformans—and observed the pronounced increase in phosphatase in both these conditions. These epochal observations led A. Riley Armstrong, Earl J. King and Robert I. Harris of Toronto to continue the studies of phosphatase in obstructive jaundice. Further contributions of interest were those made by Wm. Roberts on blood phosphatase and van den Bergh reaction in differentiation of several types of jaundice, and J. R. Thannhauser and E. Anderson—on bilirubin in blood serum thirty-one years ago.

John Browne gave one of the earliest descriptions (perhaps, one of the first) —of cirrhosis of the liver nearly 270 years ago. While Aretaeus the Cappadocian discussed "Jaundice" or Icterus, "clay-colored stools" in obstructive jaundice is mentioned for the first time in world's medical literature nineteen hundred years ago.

Glisson suffered from gallstone colic and described his attacks of pain radiating to the right shoulder and the clavicular region, and the jaundice which followed. Sir Walter Scott in his letter to Morritt dated March 1817, described his attacks of acute obstructive jaundice (cholecystitis), and also in his letter to Miss Clephane.

Richard Bright discussed jaundice and clay-colored stools, as did John Elliotson of the University of London 120 years ago. Finally, lest we forget, Hoffmann (1733), 220 years ago, first identified the phrenic nerve as the link between the abdominal and shoulder tip pains of biliary colic.

Robert Harris, of Toronto, and his associates (1934) experimentally proved the importance of the elevation of alkaline phosphatase as a diagnostic test for obstructive jaundice, and reported a series of clinical cases, which is of interest, and the modern therapy, which has brought about improvement in the so-called presently entitled nutritional deficiency in diseases of the liver, which Laennec

called "interstitial hepatitis". My friend, Professor Maurice Perrin, of Nancy, France, in 1904-1908 studied the reversibility of "alcoholic" cirrhosis of the liver, and with success used the modern day liver therapy and high dietary régime, and he noted the improvement of what we now recognize as macrocytic anemia that may occur with these diseases. Today's excellent presentation demonstrates that we are making progress in the management and diagnosis of diseases of the liver!

Dr. John R. Neefe (Philadelphia, Pa.):—I think that one first should clarify whether we are speaking of liver disease alone or liver and biliary tract disease exclusive of the problem of primary liver disease per se. Of course, many times that is the very problem one is faced with: "Which are we dealing with?"

It is my impression that biliary drainage is not used as frequently as it once was, perhaps due to the fact that there are additional methods of study now that some years ago were not available. There still remain a group of cases, for example, certain jaundiced patients in which the gallbladder does not visualize by x-ray methods, where the presence of stones may be suggested by biliary drainage.

There also have been a number of studies in which the bile has been examined for the presence of malignant cells, apparently with reasonable success. Unfortunately, a negative result means very little, although a positive result is helpful. I think it is a little difficult to define the status of this procedure any further than to say that, in occasional instances, it is of definite assistance but, due to improvements in other diagnostic methods, today it is less frequently helpful than in the past. Others, I am sure, may have a different viewpoint.

Dr. Michael A. Michaels (Manchester, N. H.):—I want to ask Dr Neefe a question. I recall a very interesting case of diagnosis of obstructive jaundice by biopsy, and I wonder how much value can be placed on that diagnostic procedure in differentiating between obstructive jaundice and hepatic jaundice?

Dr. John R. Neefe:—I think Dr. Smetana may well be able to supplement my answer to this question. I personally believe there is a great deal of difficulty in differentiating histologically some of the cases of so-called cholangiolitic hepatitis and/or cirrhosis from certain types of extrahepatic obstruction. These two groups have been the most confusing to us, even histologically. However, the ordinary extrahepatic obstructions of relatively short duration, and ordinary viral and toxic hepatitis usually can be readily distinguished.

I should be very much interested to hear how Dr. Smetana feels about this.

Dr. Hans F. Smetana (Washington, D. C.):—I had hoped to bring out these points with the slides which I presented.

In setting up criteria, one has to expose one's self, of course, and take chances of being wrong. We do believe, however, that obstructive jaundice of extra-

hepatic origin produces a distinctive pattern which is not seen in other conditions. In the early uncomplicated phase the picture is that of pure intracanalicular bile stasis without reactive intrahepatic changes either on the part of the liver parenchyma or of the structures within the portal canals. In prolonged bile stasis there may be reactive parenchymal changes or a secondary pericholangitis.

Pericholangitis is the inflammatory lesion which I discussed earlier in relation to the problem of the differential diagnosis of jaundice. Pericholangitis may be primary or secondary. It sometimes occurs as a complication of infectious hepatitis or of extrahepatic biliary obstruction. On the other hand pericholangitis may occur as a primary disease perhaps of bacterial or viral origin leading to intracanalicular bile stasis due to intrahepatic biliary obstruction in the region of the portal canals. When persistent it can go on to biliary cirrhosis. In certain cases it may be difficult to determine whether the primary event was a pericholangitis or an extrahepatic obstruction. In contrast to pericholangitis, cholangitis is the result of an ascending infection within the biliary passages, comparable to ascending pyelonephritis. We believe that these two conditions can be separated fairly easily.

There is usually very little or no histologic evidence of jaundice in needle biopsies of the liver in viral hepatitis despite marked clinical jaundice. We relate the slight degree of bile retention, seen in some instances during later phases of hepatitis to the temporary local obstruction caused by the reorganization of bile canaliculi of the hepatic cords or plates, which takes place during the regeneration of the liver cells.

Dr. Post's question concerning the significance of portal fibrosis in relation to portal cirrhosis, is most complex and very difficult to answer. I will restrict myself to saying that one can see portal fibrosis as a result of many different conditions. For instance, if the cause of a prolonged obstruction, such as a stone, is removed, a scar may remain in some of the portal canals. This, however, does not produce the physiologic consequences of a cirrhosis. Similar lesions result from healing granulomata in the liver. Since most of the granulomata are situated in portal canals, the end result of the granuloma is a scar affecting certain portal canals. This too has nothing to do with the formation and physiologic consequences of a portal cirrhosis. These and several other conditions can lead to the formation of scar tissue in the portal canal to which we refer as portal fibrosis.

Concerning the histogenesis of portal cirrhosis, we believe that the earliest lesion is the degeneration and necrosis of individual liver cells, followed by regeneration. The repeated damage to parenchymal cells and their regeneration which takes place simultaneously in varying parts of all or most lobules, finally leads to the formation of structures which are unlike normal liver lobules. These pseudolobules are composed of regenerated liver cells which are concentrically arranged and are surrounded by fibrous tissue of the former portal canals. No

regularly placed efferent veins are recognized in the pseudolobules. The fibrous tissue surrounding them contains persistent and perhaps additional, newly formed biliary passages seeking to establish connection with the bile canaliculi of the regenerated liver cells. The original reticulum about the liver cells is being gradually replaced by collagen fibres thus completing the transformation into a micronodular organ. The lack of regular drainage of the blood through the pre-existent efferent veins leads to a direct communication between the portal and hepatic veins thus resulting in intrahepatic portocaval shunts. We do not believe that the tissues of the portal canals play any significant part in the actual histogenesis of portal cirrhosis.

POSTOPERATIVE ABDOMINAL DISTENTION*

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That appreciable gastrointestinal dysfunction with subjective and objective manifestations of altered physiology occurs after abdominal operations in almost every instance has long been recognized. The roentgen confirmation of this intestinal amotility following celiotomy, by Davis and Hansen in 1945, was interesting but not startling. On the other hand the catastrophic sequelae of unrelieved intestinal distention are not sufficiently emphasized, and the necessity for the prevention of even subclinical degrees of prolonged distention is not generally appreciated.

Let us briefly review some of the fundamental mechanisms of this dreadful complication, the early and remote, local and systemic effects. Postoperative intestinal distention is ultimately the result of two principle phenomena: involuntary aspiration and accumulation into the gastrointestinal tract of excessive atmospheric air, and transient intestinal paresis, both of which, for as long as 72 hours or more, remain within reversible physiological limits. In the untreated cases the reaching or passing of critical points is a fortuitous circumstance, depending on the exaggeration or prolongation of the two phenomena mentioned. The normal curvature at the ends of intestinal loops as they are arranged within the peritoneal cavity may, by distention, be transformed into a sharp kink, which then becomes a mechanically obstructing barrier, causing more distention. In another fashion a violent attempt by a loop to propel its contents may result in a traction loop (garden hose) producing another mechanical relative occlusion of lumen, increasing the distention. A short segment of bowel may become so paretic that its very existence in the path of more normal bowel breaks up or renders nonpropulsive initially effective peristaltic waves, and acts as if it were a material barrier.

Increased distention begets more paresis and vice versa—progressing insidiously to a vicious cycle. Distentions producing intraluminal pressures of 50 to 60 mm. of mercury are sufficient to bring about occlusion of small peripheral veins of the bowel wall with subsequent causation of mural edema, failure of absorption of bowel contents, more paresis, further distention, increased intraintestinal tension sufficient to effect arterial occlusion and strangulation of the local blood supply.

Even before arterial occlusion is reached, but soon after venous compression is maintained, plasma outpourings occur, cementing temporary kinks and making them more angulated, cementing temporary twists and increasing their relative

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occlusion, and finally spilling on any raw operative surfaces and causing all manner of deforming plastic adhesions, transforming "functional" distention to mechanical obstruction.

In summarizing, the local end results of these basic pathological mechanisms of distention, namely kinking, torsion, knotting, plastic exudation, deforming adhesion, mural edema and vascular strangulation are bowel wall necrosis, ulceration, perforation, and peritonitis. The systemic sequelae are dehydration, hypoproteinemia, hypochloremia, hypopotassemia, hyponatremia, embarrassed diaphragmatic breathing with consequent atelectasis and pneumonitis, nitrogen retention, renal insufficiency, peripheral vascular stasis, thromboembolism, and

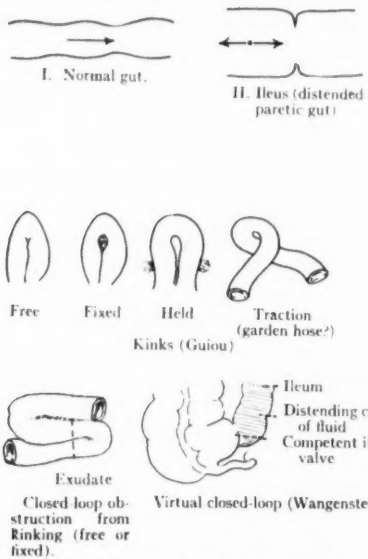

Fig. 1—The various mechanisms of intestinal distention and obstruction. *From Gius and Peterson: "Postoperative ileus and related gastrointestinal complications."*

wound disruption. The approximate chronological development of the various postoperative gastrointestinal complications is shown in Figure 4. It is obvious that at any point any dysfunction can insidiously merge into another, and beyond a certain critical point, unchecked postoperative abdominal distention becomes a self-perpetuating mechanism of destruction.

The treatment of progressive postoperative distention or established paralytic ileus is essentially much the same at that of postoperative mechanical obstruction, since these conditions are too often indistinguishable. Restoration and maintenance of biochemical balance, intestinal suction decompression by any of the large variety of long intestinal tubes, and oxygen inhalation as prescribed by

Fine and co-workers will cure the large majority of cases. It must be remembered, however, that unless recovery by these means is prompt and unequivocal according to certain established clinical and roentgen criteria, operation is in order.

Sound and clear as this dictum appears, nevertheless, it is the point on which we are beset by serious deficiencies in our knowledge and wide disagreements amongst eminent authorities. For example, we do not really know how many so-called functional distentions are actually or virtually mechanical. Again, we have no absolute diagnostic criteria that can establish or rule out the existence of strangulated obstruction. Too often, therefore, we cannot be absolutely sure of the indication for operative intervention, or the timing of such intervention. These uncertainties may in part explain for instance why an authority like Franklin I. Harris claims that 80 to 90 per cent of small intestinal obstructions are amenable to cure by intestinal intubation drainage alone, while another excellent observer like Walter F. Becker only this past October sounded the warning that this procedure as a definitive treatment is often abused, and cited a 38.4 per cent

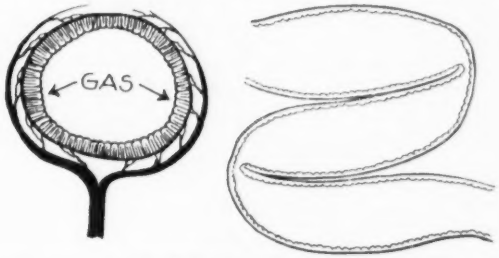

Fig. 2–Showing how increased intraluminal pressure makes smooth curves at loop ends become sharp obstructing angulations and compression of blood supply. *From John Divine: "A concept of paralytic ileus."*

mortality in 52 cases of acute adhesive ileus so treated. And finally, the most disquieting divergence is found between the credit given by American surgeons to the role of the long intestinal tube both as an ancillary and definitive agent in the reduction of mortality in intestinal obstruction and that given by Norwegian surgeons to operative interference alone in achieving similar results (since intestinal tubes have not been readily available to the Scandinavians).

When we review considerations of a choice of combinations of operative procedures and other adjuvant maneuvers, we not only find a lack of unanimity, but what is more serious, we observe in areas where this subject does not receive the attention given it, for instance, in Wangensteen's clinic, some very debatable matters of commission and omission. These are comprehensibly illustrated by the following typical examples:

1. Cases of patients with suspected paralytic ileus refractory to all conservative measures and with failure in the accomplishment of intestinal intubation.

These cases are then urgently laparotomized and upon confirmation of the diagnosis of so-called idiopathic functional ileus, the abdomens are closed, and the patients, treated only with gastric suction, succumb within a few days.

Comment:—In this type of case an intestinal tube could have been guided past the pylorus while the abdomen was open, or such a tube could be introduced through a jejunostomy or through a Wangensteen enterostomy, or combinations if any of these could be done. Certainly with distention to be relieved, it is incredible that at laparotomy not one effective therapeutic measure is carried out; yet this is not an uncommon occurrence!

2. Cases of patients with evidence of mechanical small bowel obstruction and with failure to accomplish intestinal intubation after varying periods of trial.

TABLE I

MORTALITY—ALL SURGICAL DISEASES AND OPERATIONS

Investigator	Years	Mortality Rate
Lehman & Becker	1934-1939	6.3%
	1940-1945	3.4%
MORTALITY OF INTESTINAL OBSTRUCTION		
Lehman & Becker	1934-1939	27.2%
	1941-1945	15.0%

These patients also are urgently operated upon, and obstructing adhesive bands are found and severed, releasing the obstruction. Too many of them, however, die within a few hours of unrelieved intestinal distention.

Comment:—It is evident from the examples of this class that a procedure which removes the mechanical cause of obstruction and does not relieve the distention immediately can fail to be curative. Here again, a long intestinal tube could have been passed successfully, while the abdomen was open, by any of the methods just referred to. In this connection the warning should be sounded that in this type of obstruction too much time is often lost in unsuccessful attempts at intestinal intubation.

3. Cases in which obstruction is caused by multiple small bowel deforming adhesions.

At operation these adhesions are freed and the abdomen closed. Too many of these cases then promptly become obstructed again.

Comment:—When extensive small bowel obstructing adhesions are freed numerous abrasions of the visceral peritoneum are left which invite new and

more perilous deforming adhesions. By the more frequent employment of the Noble technic of plication, these recurrences, both immediate and remote, could, in the majority of cases, be prevented.

It is claimed that the reduction of the fatality rate of intestinal obstruction in large centers has kept pace with the decline of mortality of all surgical diseases, due to the general progress in all the surgical sciences and to the application of new specific diagnostic and therapeutic advances to the problems of intestinal obstruction, as shown by Lehman and Becker in Table I.

We have come a long way from the death rate of 60 per cent for the year 1900, reported by Hawthorne and Nemir, to the rate of 11.8 per cent reported by Walter F. Becker in October 1952, from Charity Hospital, New Orleans, covering the years from 1940 to 1949 inclusive, and the present national mortality rate of 10 to 15 per cent computed by Terrell Speed in October 1952. As compared to that of other surgical diseases, however, the mortality rate of intestinal obstruction is still very high.

TABLE II

INCIDENCE OF MECHANICAL OBSTRUCTION RESULTING FROM POSTOPERATIVE DISTENTION

Investigator	Year	% P.O. Obst.	
McIver	1929-1934	Early – 11%	Of all Hosp. Mech. Obst.
		Late – 13%	
		Total 24%	
F. I. Harris	1952	Less Than 5%	Immediately Postoperatively
Sciorsci	1952	Less Than 5%	

Exactly what proportion of mechanical obstruction develops from cases having evident and serious postoperative distention is difficult to determine because most writers group both the remote and immediate obstructions without attempting a breakdown. For instance, Terrell Speed states in his article of October 1952 that the largest single group of mechanical small bowel obstructions is made up of cases of adhesive band obstructions following surgery and puts it at 33 per cent. McIver does attempt a breakdown but is not clear on what he means by "early". In a personal communication Franklin I. Harris, in referring to immediate small bowel mechanical obstructions of varying degrees of severity resulting from postoperative distention during the past five years, places them at less than 5 per cent, and my experience has been similar. Table II illustrates some of these quoted percentages.

In my opinion the incidence of both immediate and remote postoperative mechanical obstruction will be high as long as (among other things, such as infection) the incidence of postoperative intestinal distention is not decreased.

The following table shows incidence rates of postoperative intestinal dysfunction as reported up to a decade ago.

TABLE III

INCIDENCE STUDIES

Investigator	Year	Cases	% P.O. Dys.	Type of Dys.
Ottenheimer	1935	400	59%	P.O. Gas Pains
Levis & Axelman	1936	?	60-70%	Int. Atony
Gordon	1940	131	72.5%	P.O. Dist.
Noer & Johnston	1942	332	40%	Severe P.O. Dist.
Sciorsci	1936 } 1940 {	117	80%	36% P.O. Dist.

The decrease in dysfunction incidence in the past ten years or so by better prophylaxis, as will be shown later, is in my opinion, the most encouraging sign in our struggle against intestinal obstruction.

The foregoing brief survey of treatment and incidence of established ileus and mechanical obstruction and also the relation between the latter two is intended to emphasize that such treatment is a supreme test for surgeon and institution alike, that prevalent fatality rates are still very high and that their general decrease presupposes a nation-wide distribution of the unerring skill, judgment, competence and finely geared organization of leading medical centers particularly interested in this problem. On the other hand, the brief review was also intended to make obvious that within the more immediate realization of the average surgeon and institution lies the prevention of postoperative distention.

In this regard we must begin by warning that it is a fallacy to think in terms of a single preventive measure. There must be preventive maneuvers to correct or control each and every proven etiological factor of postoperative intestinal distention. Some of the more potent and generally accepted of these factors are psychic states, biochemical deficiency states, drugs, anesthetic agents, infection, trauma, and the aspiration of external air into the gastrointestinal tract. Other factors, as far as I know not mentioned, but in my experience, quite prevalent, are general bowel habit, dietary practices, and athletic condition.

PSYCHIC STATES

Much has been written, but in my opinion, little proven or clarified as to the role of fear, anxiety, and other mental states in the causation of postoperative abdominal distention. Fear and anxiety states are often over-treated with sedatives, and it is probably this over-treatment that contributes to the intestinal paresis. In my experience, people who grunt and groan with pain and discom-

fort appear especially prone to distention. It has been surprising to me that many patients who had given a history of repeated occurrence of nervous or hysterical abdominal distention did not manifest postoperative abdominal distention, as had been expected. It is my belief that there is no more unquestionable evidence for a "mental type" for postoperative abdominal distention than there is for a criminal type of Lombroso for crime or a special constitutional type of Draper for disease.

Biochemical Deficiency States

Hypoproteinemia, dehydration, hypochloremia, hyponatremia, hypopotassemia are not only initiating factors of distention but also results of continued

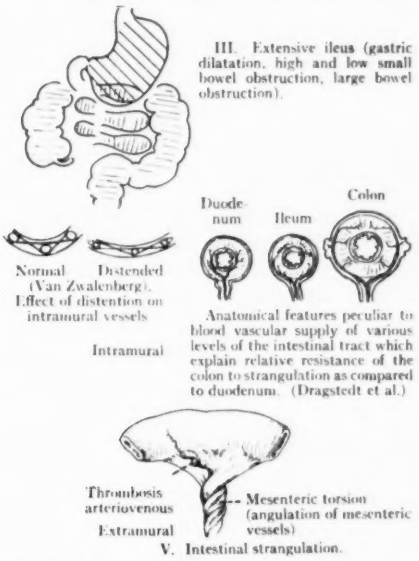
III. Extensive ileus (gastric dilatation, high and low small bowel obstruction, large bowel obstruction).
Duodenum
Ileum
Colon
Normal
Distended
(Van Zwalenberg).
Effect of distention on intramural vessels
Intramural
Anatomical features peculiar to blood vascular supply of various levels of the intestinal tract which explain relative resistance of the colon to strangulation as compared to duodenum. (Dragstedt et al.)
Thrombosis arteriovenous
Extramural
Mesenteric torsion (angulation of mesenteric vessels)
V. Intestinal strangulation.

Fig. 3—The various mechanisms of intestinal vascular strangulation—intramural and mesenteric. *From Gius and Peterson: "Postoperative ileus and related gastrointestinal complications."*

distention and therefore parts of a vicious cycle. These must be corrected in the emergency surgical patient (usually accomplished in 6 hours). Preoperative biochemical correction in elective cases should present no problem, together with the restoration of blood elements and blood volume. Deficiencies of thiamine chloride give rise to a very stubborn paralytic ileus and while the patient can be maintained in precarious compensation by intubation and the other measures, the ileus can be corrected only by the adequate replacement of this vitamin. Prevention can be accomplished only by preoperative replacement of this vitamin. All these measures are known to enhance the acetylcholine metabolism in

the intestinal wall and the administration of prostigmine is supposed to counteract the cholinesterase which destroys acetylcholine. This is the rational basis for the pre- and postoperative use of prostigmine by many surgeons. I have not found the action of this drug uniform in comparative cases and therefore have not used it extensively. Its reported merit in the hands of some investigators, however, should not be overlooked.

Drugs

The barbiturates and atrophine depress intestinal motility. The use of the barbiturates for preanesthetic sedation is wise and even helps prevent air-swallowing but thereafter they should be used most sparingly. Morphine in my opinion is still the drug of choice in relieving postoperative pain. It accomplishes this without depressing the bowel, in fact even maintaining its tone, provided its use is not too repeated and prolonged.

Anesthetic Agents

Certain agents, ether, nitrous oxides, ethylene and to some extent cyclopropane in its deeper zones depress intestinal motility. Spinal anesthesia, local and intercostal block and skillfully administered cyclopropane especially when delivered by endotracheal tube have little if any depressing effect on the gastrointestinal tract. We look hopefully to the increased use of long-acting anesthetic agents such as efocaine as a regional anesthetic, since it will eliminate pain from the operative area for many days, obviating the use of the opiates and other analgesics.

Infection

Contamination, even of the lowest grade, of the peritoneum is a notorious disruptor of normal bowel motility. The antibiotics used when indicated, and even prophylactically and routinely by many surgeons have considerably reduced this factor. The use of the sulfonamides alone, or with the antibiotics, preparatory to bowel surgery has also been a great adjuvant. It is noteworthy that these antibacterial agents have not appeared to cause any depression of intestinal motility.

Trauma

The effects of operative handling of the visceral and parietal peritoneum are well known, especially in the vicinity of great nerve centers such as the renal plexus, etc. Their prevention is accomplished by refined technic, gentle handling of tissues, and judicious use of packs and other possible abrasives.

External Air

It has been demonstrated by numerous investigators, among whom are Kantor, McIver and Wangensteen, that external air forms the greatest part of

the gaseous content of the distended bowel, and unabsorbed secretions, the fluid content. Other ingenious workers such as Morris, Ivy and Maddock have shown that the air is involuntarily swallowed or aspirated during inspiration against a closed glottis. Davis and Hansen in 1945 noted that a considerable amount of this air is taken in during anesthetic induction—as much as 2,150 c.c.—and advised gastric tube suction during anesthesia and operation to prevent air from getting beyond the stomach. They further recommended this gastric suction for periods of one or two days or more, since the abnormal air-swallowing or inspiration mechanism may persist. Figure 5 shows at a glance the approximate analysis of the gases found in distended bowel.

As I mentioned above, I have found patients who suffer from constipation, particularly the proximal colonic type, exceedingly prone to postoperative intestinal dysfunctions and distention. I have also frequently noted that people who are accustomed to a diet of coarse and spicy foods have a postoperative "intestinal motor let-up", since their bowel tract appears to receive no stimula-

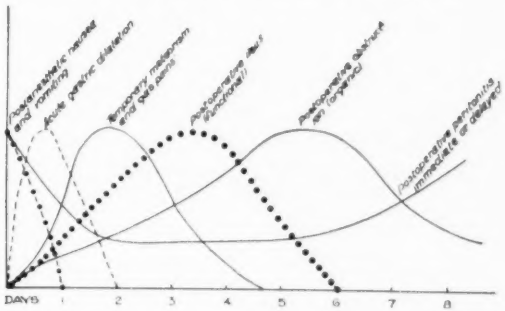

Fig. 4—The chronological development of postoperative gastrointestinal dysfunctions and complications. *From Gius and Peterson: "Postoperative ileus and related gastrointestinal complications."*

tion from bland or liquid food. Finally, I have observed that very athletic individuals or those accustomed to hard physical work are more prone to postoperative intestinal amotility or atonia because of their enforced inactivity. I have considered these groups definite candidates for early vigorous prophylaxis.

To the prophylactic measures already enumerated or implied, must be added one of the most effective in the reduction of gastrointestinal dysfunction—early ambulation. I should consider it a most difficult task if I were asked to rearrange these preventive measures in the order of their effectiveness.

At this point I should like to request your kind indulgence as I devote perhaps a disproportionate amount of time to the presentation of a prophylactic maneuver, which in my opinion merits more than the meagre attention it has received. In the latter part of 1945 we found that about 40 per cent of the patients, in whom there were definite indications for prophylactic gastric tube suction,

as just referred to, refused or willfully discontinued this procedure; while others who bravely attempted to endure it, evinced anxiety states and discomforts apparently outweighing the advantages. This situation posed a challenge for an alternative method.

For many years previously I had been impressed by the spasmodic tightness of the anal sphincter in severe postoperative abdominal distention. On the other hand, I had been intrigued by the absence of postoperative distention in patients deliberately constipated by diet and medication as part of the postoperative regimen in hemorrhoidectomy, anal fistulectomy and other rectal operations, in all of whom gentle but complete manual dilatation of the sphincter ani immediately preceded the operation. I had also observed that contrary to the behavior of these rectal cases, many perineal and vaginal plastic operations, also similarly deliberately constipated for three to five days as part of a postoperative nonsoiling routine, but not undergoing anal sphincter dilatation, displayed varying de-

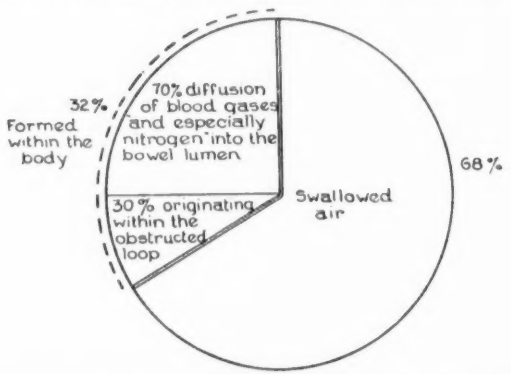
32%
Formed within the body
70% diffusion of blood gases and especially nitrogen into the bowel lumen
30% originating within the obstructed loop
68%
Swallowed air

Fig. 5—Origin of intestinal gases in distention and obstruction (Owen Wangensteen).

grees of postoperative abdominal distention. In these contrasting behaviors, lay the hint that the difference was brought about by the dilatation of the sphincter ani. It then occurred to me that deliberately paralyzing the sphincter ani by thorough manual dilatation might remove with precise timeliness the last barrier of resistance, as it were, in the gastrointestinal tract, thus converting what would have been ineffectual intestinal contractions into effective ones against the lowered or effaced terminal resistance. This reasoning appeared plausible even in terms of the Alvarez' gradient theory of intestinal propulsive activity, and the Alvarez-Hosoi theory of the leveling of the intestinal gradients in intestinal distention, for which they suggested the term "flat-gradient ileus". Furthermore, it was recalled that in 1938 J. K. Donaldson had reported that stimulation of the sphincter ani caused reflex stimulation of the sympathetics thereby predisposing to inactivity and distention of the bowel. Tight spasmodic sphincters were considered as possessing a self-stimulating mechanism.

Accordingly by the end of 1945 the anal dilatation maneuver was employed in the previously mentioned 40 per cent of cases not receiving intragastric intubation and suction, and while these patients presented the indications for such intubation, the results obtained by dilatation compared very favorably with those achieved by suction.

The dilatation is performed immediately upon completion of all abdominal operations, carefully, gently, and gradually, avoiding haste and trauma, thoroughly stretching the sphincter muscle fibres to the point of admitting practically the entire hand. In the case of children, dilatation to 3 or 4 fingers is maximum. Gas often escapes during this maneuver. A careful dilatation which paralyzes the sphincter for 2 to 5 days, rendering it unable to oppose any resistance to the escape of gas, takes about 2 to 5 minutes of the remaining anesthesia. Dilatation is easiest under spinal anesthesia. We have noted at no time any unfavorable immediate or remote sequelae.

We have, therefore, since late 1945 employed this prophylactic measure routinely immediately upon completion of all abdominal operations, whether

TABLE IV

SCIORSCI—ST. FRANCIS HOSPITAL

Year	Cases	Total P.O. Dysfunction
1936-1940	117	80%
1941-1944	312	48%
1945-1952	802	31%

the gastric tube was used or not. As we continued to record its benefits we used the gastric tube even less, so that in all, the proportion has been about 5 dilatations to 1 intubation, with results summarized in Tables IV and V.

Reduction of total postoperative dysfunction (including gas pains, nausea and vomiting, abdominal distention) from an incidence of 80 per cent to 48 per cent over the 1940-1944 period must be ascribed mainly to early ambulation and chemotherapy. Further reduction of total postoperative intestinal dysfunction to 31 per cent by the end of 1952 must be credited to the combined uses of early ambulation, chemo- and antibiotic therapy, gastric suction as just described, and anal dilatation, which, in many cases, sufficed without the use of the other measures, proving over and over again its adequacy. The breakdown of the postoperative dysfunction figures is shown in Table V.

Evidently the same reasons can account for the reduced incidence of gas pains to approximately ⅓, nausea and vomiting to approximately ½, postoperative abdominal distention to ⅛, and the need for operative intervention for ileus to about ⅛ of their 1936-1940 occurrence. Similarly accounted for are other noted

benefits such as earlier passage of flatus (sometimes within the first 8 to 12 hours postoperatively), earlier spontaneous or unaided bowel movements (first to fourth days postoperatively), and earlier return of normal peristaltic sounds, together with a significant reduction in the amount of postoperative sedatives and analgesics used.

The possible application of efocaine infiltration in the operative area and also in the region of the sphincter ani as an adjunct to the prolongation of prophylactic sphincter dilatation should be explored.

Up to recently I believed myself alone in the employment of this procedure as I had found no mention of it in the literature, until I came across an article in the *American Journal of Surgery* for April 1929, by the late Dr. Angelo L. Soresi, a brilliant New York surgeon, scientist and inventor, who reported the routine employment of anal sphincter dilatation in all laparotomies with satisfactory results comparable to mine. It must be noted that he achieved these results from 1920 to 1929 before the development of our present surgical and

TABLE V

SCIORSCI– ST. FRANCIS HOSPITAL

Year	Gas Pains	Nausea & Vomiting	Postoperative Distention	Operative Intervention
1936-1940	84%	57%	60%	9%
1941-1944	68%	40%	32%	3%
1945-1952	34%	27%	10%	1.4%

medical armamentarium. He definitely recommended the procedure and emphasized that he had encountered no ill effects.

Further research disclosed, though rather vaguely, the use of this maneuver by Dr. Charles W. Mayo of Rochester, Minn., but no published account. In reply to my inquiry Dr. Mayo promptly sent the following personal communication:

"I have been dilating the anus in all cases of large and small bowel lesions in which an incision has been made in the bowel or in which resection and anastomosis have been performed, and also, less frequently, in other cases. My father, who was Dr. Charles H. Mayo, also did so.

"It is difficult to give anything more than impressions regarding the procedure and it would be almost impossible to make an exact study. I have not seen any complications result from it and it is my opinion that it has been a helpful procedure; at least, the cases have been few on our service in which the Miller-Abbott tube has been required as a postoperative measure. I would think that it would be a particularly valuable procedure for a nervous type of patient or one who complained preoperatively of gas."

After failing to find other references to this subject in the surgical literature, I did what many others have done—request information of that Dean of American Surgeons, Dr. Rudolph Matas. In his reply, Dr. Matas wrote, "Of course the dilatation of the sphincter ani has been resorted to for innumerable procedures, but not so generally known or appreciated as a preventive or prophylactic measure especially after abdominal and anorectal operations. I believe, however, that your systematic use of this procedure has not been sufficiently appreciated or its merit recognized, and you have rendered a valuable service, indeed, by attracting attention of the profession to its value."

In conclusion, the destructive self-perpetuating mechanisms of postoperative intestinal distention have been reviewed, the urgent need for their complete prevention emphasized, and an outline of preventive measures based on counteracting all proven etiological factors has been offered, together with the description and results of a maneuver which is believed to merit wider acceptance.

EDITORIAL

Esophageal Varices

About a century ago, Diberder and later Fauvel reported cases of esophageal varices. Formerly, it was believed that varices of the esophagus occurred at rare instances. It has been only since the development of a technic by which the mucosal relief of the gastrointestinal tract could be studied that a number of such cases began to appear in the literature.

Up until 1880, only 3 additional cases were reported independently of each other by Dusaussay, Chautemps and Ledoc. Ledoc called attention to a case of hepatic cirrhosis, syphilitic in origin, resulting in thrombosis of the portal vein and veins of the stomach. In 1907, Gilbert and Villaret reported a case similar to that of Ledoc and, not until 1887, did a report of esophageal varices appear in the American literature. This report of Van Bibber was published in the Maryland Medical Journal and 10 years later, the importance of this condition was stressed by an editorial appearing in the Medical Record.

In 1900 Proble, in 1920 Blumenau and in 1928 McIndal, called attention to deaths caused by advanced portal cirrhosis, gastrointestinal hemorrhage and ruptured esophageal varices.

In the proceedings of the Mayo Clinic, 1933, Rivers reviewed 668 cases of hematemesis and he found that 90 per cent were caused by intrinsic gastroduodenal lesions, while for extrinsic lesions, cirrhosis of the liver occurred in 1.8 per cent and splenic anemia in 2.8 per cent. The most common cause of bleeding in these two conditions was esophageal varices.

A three and one-half year old child who died from hemorrhage, was found at postmorten to have had extensive erosions of a dilated esophageal varix without other lesions, especially cirrhosis of the liver.

To understand the formation of esophageal varices, a review of the anatomy of the venous system of the esophagus and the portal system is necessary. Interference with the circulation of the portal system will often lead to dilatation of the veins of the esophagus. These veins are gathered into a plexus on the outer surface of the esophagus, which receives its blood from the walls of the tube. From the lower portion of the plexus, small branches go to the coronary vein of the stomach while higher up branches drain into the azygos and thyroid veins. Thus, an anastomosis is formed between the portal and systemic veins.

A special study by Kegaries of the venous plexus of the esophagus showed that very small venules form the anastomosis between the portal and systemic circulation, especially at the cardiac end of the stomach and in cases of portal obstruction, varices result from the increased flow of blood through the vein which is unable to withstand the increased venous pressure. He stressed the connection between the splenic and esophageal veins via the vasa brevia.

It is quite possible that varices of the esophagus may develop independently of cirrhosis of the liver, particularly in the presence of diseases of the spleen, such as splenic anemia or Banti's disease. Diminution in the size and number of the blood sinusoids of the spleen obviously interferes with the outflow of blood from that organ, thus necessitating the establishment of collateral circulation.

Varices due to portal obstruction usually develop in the lower third of the esophagus, and in spite of the general congestion of the gastrointestinal tract, hemorrhoids are seldom observed. This phenomenon may be explained by the possible antagonism between esophageal and hemorrhoidal veins.

Pathological conditions, which may be the forerunners of esophageal varices, are: cirrhosis of the liver, syphilis of the liver, thrombosis of the vena porta, thrombosis of the splenic vein, tumor in the region of the vena porta, tumor of the pancreas and even achalasia of the esophagus.

If there is interference in circulation in the superior vena cava, varices are likely to form in the upper third of the esophagus. A tumor of the mediastinum, causing pressure on the trachea and superior vena cava, may also cause varicose formation in the upper esophagus. Well developed varices appear as irregular, tortuous, rounded, nodular elevations, dark blue in color and covered by mucosa. They are thin-walled, extend longitudinally, and their diameter may reach the size of a pencil.

Varices of the esophagus occur usually after the age of forty and are found equally in both sexes. They have been found also in the new born and very young, the latter must be considered congenital.

Symptomatology:—Weakness, shock, fullness in the epigastrium, hiccough and occasionally gastric colic may occur. None of these findings, however, are characteristic or constant. The one symptom which is characteristic but seen only after rupture is hemorrhage, often so profuse as to cause death.

As a result of rupture and consequent hemorrhage, recurrent hematemesis may occur, but here again many cases do not present this sign. Instead, the picture may be that of weakness, fullness in the epigastrium associated with tarry stools, often leading the physician to suspect gastric or duodenal ulcer, gastric malignancy, leukemia, malaria, hemophilia and even vicarious menstruation. The autopsy surprisingly shows ruptured esophageal varices. The presence of acute esophagitis found at necropsy is no doubt a prerequisite of hemorrhage from the submucus venous plexus which lies just beneath the avascular epithelial coat of the esophagus. Therefore, it is quite susceptible to ulceration, rupture and hemorrhage. Passive congestion and vomiting of acid gastric juice may be considered to be additional prerequisites.

In the diagnosis of esophageal varices, the only safe method is by careful roentgen-ray study of the mucosa of the esophagus. In mucosal study of the

esophagus in supposedly normal patients, the examiner observes two or more longitudinal rugae running parallel to each other and continuing into the rugae of the lesser curvature of the stomach. This pattern is absent if varices are present. In addition, the esophagus shows multiple round and oblong filling defects, tortuous, net-like bands of decreased density; these are caused by the enlargement of the vessels which protrude into the lumen and are projected above each other. There is also a widening of the diameter of the esophagus, probably due to the mass of vessels lying in its lumen.

When the varices are small, the diagnosis is more difficult and the mucosa must be examined very carefully in all directions. While the study of the mucosal relief is so important, the complete filling of the esophagus should not be omitted. It is necessary as a means to judge the elasticity of the organ; to study the relationship of the different parts of the digestive tract to adjacent organs.

In the differential diagnosis between esophageal varices, malignant and benign tumors, hemangioma and hiatus hernia with bleeding, the examiner must take into consideration that superficial fluoroscopic observation may be, in the presence of air bubbles or particles of food, mistaken for a lesion. Multiple papilloma is very rare but may resemble varices and be mistaken for it. Repeated fluoroscopy and films may help to differentiate the two conditions. When varices are present, they are snakelike in appearance while papilloma are rather flat.

The most important question in differential diagnosis is carcinoma. Carcinoma, however, usually occupies a circumscribed position while varices are more diffuse and extensive. It is extremely important to observe the elasticity of the wall while it changes shape with respiration and with the action of the heart. Absence of elasticity may mean infiltration of the wall, inflammatory or neoplastic in origin. If the lesion which appears like a varix is in the region of the bifurcation, we must think of a neoplasm as this locality is a favorable one for carcinoma. Here again, careful and repeated examinations and esophagoscopy are necessary in order to avoid error.

In periesophagitis the spur-like distortions on the wall of the esophagus may simulate varices, but the atypical location in the mid-section of the esophagus, together with the normal mucosal pattern, excludes varices. Cardiospasm occasionally causes an irregular motor play which imparts a wavy appearance to the contour of the esophageal wall, assuming a resemblance to varices. Here again, accurate fluoroscopy with the study of the mucosal pattern simplifies the diagnosis.

In treating esophageal varices, it is important that a definite diagnosis be established and determined whether or not there is interference with the portal circulation (cirrhosis of the liver or Banti's disease). In this way, many cases of esophageal varices may be detected. In varices, especially those due to cirrhosis of the liver, a high carbohydrate nonirritating diet is indicated. Spices, alco-

hol, coffee and extremes in temperature of foods or drinks are to be avoided. The use of stomach and duodenal tubes and other instruments is especially contraindicated. In order to avoid a sudden rise in blood pressure, the patient should do the minimum amount of exercise, abstain from straining during defecation and adequate sedation should be administered if a cough is present. The underlying pathology should receive the proper medical or surgical treatment.

SAMUEL WEISS

CHAPTER ACTIVITIES

Boston Chapter

A meeting of the Boston Chapter of the National Gastroenterological Association was held at the Boston City Hospital on 28 January 1953.

The speakers were Dr. Thomas P. Almy, Associate Professor of Medicine, Cornell University School of Medicine, whose subject was "Modern Concepts of Ulcerative Colitis" and Dr. Leland S. McKittrick, Clinical Professor of Surgery, Harvard Universtiy School of Medicine, whose subject was "Surgical Aspects of Ulcerative Colitis".

New Jersey Chapter

At a meeting of the New Jersey Chapter of the National Gastroenterological Association on 12 January 1953, Dr. I. Gelber of Elizabeth presented an interesting collection of small bowel lesions with case reports and illustrations. Dr. F. Weisbrod of Newark presented two cases of lesions in the esophagus.

New York Chapter

The New York Chapter held a meeting at the Academy of Medicine in New York on 12 January 1953 at which the speakers were Drs. Michael Weingarten, Gordon McNeer and Oscar Bodansky.

At a meeting of the Chapter held 9 March 1953 the speakers were Dr. Jacob Buckstein and Dr. Robert S. Sherman.

The next meeting of the Chapter will be held on 13 April 1953.

The annual meeting of the Chapter will be held on Monday, 11 May 1953 and will be preceded by a dinner in honor of Dr. Roy Upham, Secretary-General of the National Gastroenterological Association.

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NEWS NOTES

Eighteenth Annual Convention

Hotel reservation cards for the Eighteenth Annual Convention of the National Gastroenterological Association, which is being held at the Hotel Biltmore in Los Angeles, Calif., 12, 13, 14 October 1953, were mailed to members of the Association with the March issue of the Bulletin.

Non-members may obtain the reservation cards from the Secretary, 1819 Broadway, New York 23, N. Y.

The program for the convention and the Course in Postgraduate Gastroenterology which follows the convention is rapidly being completed and will be published in the September 1953 issue of The Review of Gastroenterology.

Course in Postgraduate Gastroenterology

The Fifth Annual Course in Postgraduate Gastroenterology sponsored by the National Gastroenterological Association will be given in Los Angeles, Calif., on 15, 16, 17 October 1953, immediately following the Eighteenth Annual Convention.

As in the past the directors and co-chairmen of the Course will be Dr. Owen H. Wangensteen, Professor of Surgery and Chairman of the Department of the University of Minnesota Medical school and Dr. I. Snapper, Director of Medical Education, Cook County Hospital and Professor of Medicine, Chicago Medical School.

The faculty for the Course will be selected from amongst the medical schools in and around California. In addition to lectures there will be one session devoted to clinics at the College of Medical Evangelists in Loma Linda.

The fee for the 3 days will be $50.00 for non-members of the Association and $35.00 for members of the Association.

Further information and an application blank may be obtained by writing: Dept. R. G., National Gastroenterological Association, 1819 Broadway, New York 23, N. Y.

Executive Committee Meeting

A meeting of the Executive Committee of the National Gastroenterological Association was held in New York City on 18 January 1953.

Routine communications were presented and disposed of.

The Association was advised of the deaths of Dr. W. G. Colvin, Grand Rapids, Mich.; Dr. Lawrence J. McCarthy, Boston, Mass. and Dr. Alberto Navarro of Panama. The Secretary was instructed to send letters of condolence.

The names of Drs. Rene Gutmann of Paris, France and Rudolf Nissen of Basel, Switzerland were submitted to the National Council for election to Honorary Fellowship in the Association.

Nominations to fill the vacancies on the Sub-Specialty Board of Gastroenterology of the American Board of Internal Medicine were forwarded to the Secretary of the American Board of Internal Medicine.

Dr. Roy Upham, Secretary-General, reported on the activities of the Boston, New Jersey and New York Chapters. He also reported that two regional meetings, one for the South and one for the Central region, had tentatively been scheduled.

The Treasurer, Dr. Elihu Katz, presented a financial statement for the Association as well as an estimated budget prepared in conjunction with the Committee on Finance and Budget. The Treasurer requested that those members who have not paid their dues for 1952 be dropped from the roster of the Association.

The New York Chapter presented for ratification the applications of the following, which applications were approved by them and accepted by the Executive Committee: Dr. Morris H. Cohan, Brooklyn, N. Y.; Dr. Jules D. Gordon, New York, N. Y.; Dr. Adolf Kornstein, Brooklyn, N. Y.; Dr. Henry Litinsky, Staten Island, N. Y. and Dr. Theodore Tuller, New York, N. Y.

The applications of the following were accepted for membership at large in the National Gastroenterological Association: Dr. Paul Andrew Blackstone, Mansfield, Ohio; Dr. Peter G. Brandetsas, Palmyra, N. Y.; Dr. James Chakmakis, Lewiston, Maine; Dr. Edward Walter Chudzik, Garfield, N. J.; Dr. Victor Curatolo, Detroit, Michigan; Dr. B. Drewniany-Killeen, Lyndhurst, N. J.; Dr. Heinz Eisenstadt, Port Arthur, Texas; Dr. Donald G. Francy, Lyndhurst, N. J.; Dr. Leslie Miller, Belleville, N. J.; Dr. Morris Charles Miller, Montreal, Canada; Dr. Oscar Rogol, Seymour, Conn.; Dr. Wallace Spigel, Norfolk, Virginia and Dr. Harold S. Yood, Plainfield, N. J.

Upon presentation of the necessary qualifications, the following were advanced as indicated: Dr. Max S. Konigsberg, New York, N. Y., Associate Fellow and Dr. Victor Willner, Woodmere, N. Y., Fellow.

The Editor, Dr. Samuel Weiss, reported on the status of THE REVIEW OF GASTROENTEROLOGY discussing the financial and publication aspects.

Dr. C. Wilmer Wirts, reporting for the Editorial Policy Committee, advised that, in the opinion of several other medical editors, no change should be made in the format of the journal.

The Program Committee reported progress in arranging the program for the convention and Postgraduate Course.

Several proposed amendments were submitted to the Committee on Constitutional Revision for their consideration.

Dr. Sigurd W. Johnsen, Chairman of the Administrative Advisory Committee, presented a written report of the Committee's survey of the Executive Office. Amongst the recommendations were: an amendment to the By-Laws setting forth the duties and responsibilities of the Executive Officer, authorizing additional personnel for the Executive Office and suggestions for changes in the budget.

In view of the difficulties encountered at the Hotel Statler during the 1952 convention, it was decided to cancel arrangements already made there for 1956 and obtain accomodations at the Hotel Roosevelt in New York City.

The Executive Committee selected Boston, Mass. as the site for the 1957 convention.

It was pointed out that an error in Life Fellowship fees existed in that the $100.00 fee was for ages 60 to 70. This was rectified to read: "Life Fellowship fee is $100.00 for those 60 years of age and over".

Dr. Arthur Kirchner reported by mail that the American Academy of General Practice has recognized the Course in Postgraduate Gastroenterology for informal credit and that steps will be taken to have the Course approved for formal credit.

In Memoriam

We record with profound sorrow the passing of Dr. Lawrence J. McCarthy, Member, Boston, Mass.; Dr. Alberto Navarro, Associate Fellow, Panama City, Panama and Dr. Aurel Gilbert Lavoie, Fellow, Springfield, Mass.

Our deepest sympathies are extended to the bereaved families.

ABSTRACTS

GASTROINTESTINAL TRACT

ROENTGENOLOGIC EXPLORATION OF GASTRIC RUGAE WITH REFERENCE TO THE DIAGNOSIS OF GASTRITIS: W. P. Stampfli. Radiology 59:336, (Sept.), 1952.

Stampfli's films of the rugae of the stomach belong to the best illustrations, published in this field. He uses one ounce of a fairly thick barium mixture, which the patient swallows while standing. The patient is turned in all directions, the examiner spreading the opaque material over the palpable portion of the stomach and attempting to get some of it into the first part of the duodenum. The table is then tilted backward. Excess barium gravitates up and posteriorly to the fundus, while air passes to the antrum and may enter the duodenum. Films are taken in different diameters and in different positions. Roentgen methods have been considered inaccurate in the diagnosis of gastritis. Stampfli believes that with continued interest in the problem by radiologists, better understanding will result, and better diagnostic criteria will become available. Normal rugal anatomy is described and an attempt is made to show how inflammatory disease might change the appearance of the mucosal folds.

FRANZ J. LUST

PROBLEM OF PATHOGENESIS OF CHRONIC HYPERTROPHIC GASTRITIS: W. B. Dublin. Radiology 59:377, (Sept), 1952.

Chronic hypertrophic gastritis, duodenitis, and gastric and duodenal ulcer are regarded as manifestations of the same general process: vagal hyperfunction. Localization and type of injury and repair are affected by local factors, such as variation in vascular architecture and tissue resistance. Especially in the pyloric region, the hypertrophied muscularis may join contiguous submucosa in fibrosis; in this way, the firm ring of tissue is formed which is encountered in the condition referred to as antral gastritis. The fibrotic, thickened prepyloric muscle may lead toward the hypertrophied pyloric sphincter as a gradually thickened cuff, incorporating the sphincter, or in some cases ending just proximal to the sphincter, leaving a small intervening notch or segment of muscularis which is of relatively normal thickness. The proximal portion of the stomach may appear relatively normal; more often, there is at least some degree of chronic inflammation. The mucosal surface shows nodular irregularity. The intrinsic mucosal structure may be altered: except in cases of atrophy, the parietal cells appear reasonably numerous and capable of forming acid. Lymphocytic infiltration may appear, especially in mucosa and submucosa. The latter may be edematous and fibrosed.

FRANZ J. LUST

PATHOLOGY OF GASTRITIS: L. W. Larson, and R. R. K'ing. Radiology 59:371, (Sept.), 1952.

Except for the difference in the size and number of the glands, the microscopic features of chronic gastritis are fundamentally the same whether the mucosal folds are larger or smaller than normal. The essential features are infiltration with inflammatory cells and alterations of the epithelial tissue. An exudative reaction may occur, however, which presents different histological findings from those described above. Here, polymorphonuclears appear in large numbers, particularly in the upper mucosa. There is a concomitant diminution in the mucus vacuolization which may extend well down into the glands. Russels' bodies are increased. This exudative reaction may be superimposed on any of the above described types of reaction.

Numerous attempts have been made to correlate the gastroscopic, radiologic, and pathologic findings in gastritis. To date, these have not been entirely successful. There are seven illustrations to this article.

FRANZ J. LUST

DETECTION OF GASTRIC CARCINOMA BY PHOTOFLUOROGRAPHIC METHOD: F. J. Roach, R. D. Sloan, and R. H. Morgan. Am. J. Roentgenol. 67:68, (Jan.), 1952.

The authors report a definite failure of the photofluorographic method to be of practical value in reducing the death rate from gastric malignancy. In 29 months, they examined 10,000 patients at The Johns Hopkins Hospital, 40 years of age and over. The number of individuals with early neoplastic disease is relatively small, being one per 476 examinations, or 0.2 per cent in their series. Furthermore, it has been experienced that only a few of these can be persuaded to submit themselves to surgery prior to the development of symptoms. In this series, 1,209 cases, or 13.3 per cent, had standard gastrointestinal series in addition to the miniature studies. In this group there were only 17 cases in whom the miniature studies were interpreted as showing a normal stomach, only to have the standard examination reveal the presence of gastric pathology. The false positives were 25.4 per cent. The true incidence of gastric pathology in this series is difficult to evaluate. If one takes only those cases in whom lesions detected by the miniature studies were actually confirmed by standard examinations the over-all incidence is 1.3 per cent, or 1 in 79 examinations. In 47.8 per cent the duodenal bulb was inadequately visualized for diagnostic purposes. It shows that one thorough examination is better than many mass examinations.

FRANZ J. LUST

PERIGASTRIC ADHESIONS AND BANDS INVOLVING THE PYLORIC ANTRUM: E. L. Jenkinson, W. H. Pfisterer, R. C. Norman, and K. K. Latteier. Am. J. Roentgenol. 67:210, (Feb.), 1952.

Lesions of the pyloric antrum are of equal interest to the diagnostician and the surgeon. Close cooperation is essential to identify such lesions early. Should the conclusion leave any doubt as to the presence of a malignant or potentially malignant lesion, surgery is advisable. Prepyloric defects that persist after administration of antispasmodic and medical management should be subjected to surgery. To find no lesion at operation in the presence of persistent roentgenological defect is definitely better than at a later date to find an inoperable malignancy. Persistent roentgenological defects do occur in the absence of surgical proof. In the light of the authors' present knowledge, it is often impossible to differentiate, clinically or roentgenologically, pyloric defects. Unfortunately, gastroscopic examination does not clarify the diagnosis. Several roentgenograms and drawings of the operative findings in perigastric adhesions illustrate the article.

FRANZ J. LUST

ANTRAL GASTRITIS: H. M. Berg. Radiology 59:324, (Sept.), 1952.

The roentgenological changes seen in antral gastritis are (1) hypersecretion, (2) pylorospasm, antral spasm, and narrowing of the antral region, (3) shortening of the antral region due to contraction of longitudinal muscles, (4) Gastric folds usually enlarged, sometimes with polypoid appearance. (Some cases are seen, in which the mucosa is smooth, as in scirrhous carcinoma) (5) Stiffness of folds in the antral region due to infiltration of the submucosa. (Folds do not flatten out on pressure and do not thin out with peristalsis.) (6) Irregularity of peristalsis in antral region. (7) Prolapse of gastric mucosa into the duodenum. (8) Hypertrophy of pyloric musculature in some cases. (9) Delay in emptying time of the stomach due to antral spasm and pylorospasm. (10) Small ulcer craters sometimes detectable in involved areas. The most important fact is the appearance of the gastric mucosa. In gastritis, the folds cross the affected area without interruption. The author reports 59 cases. In eleven cases, the diagnosis was that of a probable cancer, however, further studies and the course of the disease revealed the benign nature of the lesion. The article is well illustrated, spot films are demonstrated.

FRANZ J. LUST

ESOPHAGUS

CURE OF A STRICTURE OF THE ESOPHAGUS OF CAUSTIC ORIGIN AFTER GASTRIC RESECTION: C. Auguste. Arch. mal. app. digest. 41:905, 1952.

The author reports the first known example of a stricture of the esophagus of caustic origin being cured after gastric resection.

The patient, who is now 55, in May 1942 swallowed a mouthful of concentrated washing soda. Three months later, there was almost complete dysphagia: radiological examination revealed a close stricture of the lower half of the esophagus, and esophagoscopy showed a scarred membranous funnel ending in a filiform opening, 31 cm. from the dental arches. The dilatation enabled the patient to be fed fairly rapidly afterwards, but in December 1942 he underwent gastric resection, as he was suffering from intolerable gastric burns apparently due to the gastric lesions brought on by the caustic. The gastric secretion which had been hyperhydrochloric became anhydrochloric following the operation.

Dilatation was resumed as soon as the patient recovered. The size of the aperture of the esophagus had already diminished but progress was rapidly made by bouginage, and two months later it was possible to introduce a number 40 French bougie. For 18 months the passage of the number 40 French bougie was continued, then all treatment was abandoned in 1944.

When seen again in March 1952, the patient was clinically cured. He could swallow solid foods and liquids more easily than in 1944; the diameter of the esophagus had not varied; radiological examination and esophagoscopy gave no indication of the existence of the lesions observed in 1942. The general condition was excellent.

The author submits that such an exceptional cure cannot be due solely to the effect of the dilatations and must be attributed to the additional action of the gastric resection. The most probable explanation is that the operation stopped gastroesophageal regurgitation which was maintaining a latent peptic esophagitis, interfering secondarily to aggravate the sequelae of corrosive esophagitis.

The hypothesis is not unlikely in the case of this patient who bore lesions of the lower esophagus likely to obstruct evacuation of the stomach whose secretions had conserved a high acidopeptic strength until the operation.

The reported observation favors the opinion of Wangensteen, who, in 1949, proposed treating strictures of the lower esophagus of caustic origin by gastric resection.

STOMACH

CARCINOMA OF THE CARDIA OF THE STOMACH AS DETECTED BY LAMINAGRAPHY: R. L. Friedman, and M. G. Wasch. Am. J. Roentgenol. 67:932, (June), 1952.

Thirteen cases of carcinoma of the stomach are reviewed with an evaluation of air insufflation of the stomach with routine and laminagraphic studies as a means of earlier diagnosis of carcinoma of the cardiac end of the stomach. Of these, ten revealed definite evidence of the tumor, six of which were confirmed by laparatomy; the symptomatology and course of the remaining four cases were clinically beyond doubt. There were three failures by this method: one proved to be cirrhosis of the liver, in the second instance, a patent pylorus prevented a satisfactory outline of the cardia; the third and most disconcerting error was due to a flat serpigenous neoplasm which failed to encroach sufficiently upon the gastric lumen. The method of visualization of the tumor by means of laminagraphy is described. The scalloped margin of the tumor mass, as visualized on the laminagraphic study, is stressed as of diagnostic importance in differentiating an intrinsic tumor mass from extrinsic pressure on the air-filled cardia of the stomach.

FRANZ J. LUST

INTESTINES

ROENTGENOLOGICAL EXAMINATION AND EVALUATION OF THE ILEOCECAL VALVE: C. L. Hinkel. Am. J. Roentgenol. 68:171, (Aug.), 1952.

The ileocecal valve can and should be identified and evaluated in essentially every barium enema roentgen examination. This is readily accomplished when barium is introduced into the terminal ileum and graduated pressure is applied to this area. The appearance of the filling defect at the valve orifice is dependent upon the size of the

implantation, the size, shape and thickness of the lips, and the degree of prolapse of ileal mucosa. There is a wide range of variation. Several factors which tend to produce conspicuous defects are presented, together with two cases of presumably ileal prolapse, which were surgically explored. The authors believe that preparatory catharsis exaggerates the filling defect produced by ileal prolapse. Not all large or peculiarly shaped defects can be differentiated with certainty from tumors of the valve lips.

FRANZ J. LUST

PARENCHYMAL AMEBIASIS: A CLINICAL STUDY: M. J. Freedman, E. A. Cleve. Am. J. M. Sc. 224:659-666, (Dec.), 1952.

From this study it was concluded that the diagnosis of intestinal amebiasis and its complications may at times be most difficult. Because patients infected with e. histolytica often undergo dramatic cures with proper therapy, a high index of suspicion should be maintained whenever suggestive symptoms occur. Therapeutic trial is often indicated in absence of a proven diagnosis. There are presented cases illustrative of hepatic amebiasis, pulmonary amebiasis, brain abscess, and gastrointestinal complications.

J. R. VAN DYNE

PARTIAL OBSTRUCTION OF THE SMALL INTESTINE—WITH SPECIAL REFERENCE TO THE OBSTRUCTING SEGMENT: F. J. Martin, and H. L. Friedell. Radiology. 59:49, (July), 1952.

The roentgen diagnosis of partial obstruction of the small intestine has been discussed with special reference to changes which aid in localizing and studying the obstructing segment. The anatomical changes in the segment proximal to the lesion may indicate that a partial obstruction is present. One or more of the following abnormalities may be identified: (a) gas within the lumen of the small intestine, (b) an increase in the caliber of the small bowel as identified by either a barium mixture or intraluminal gas, (c) abnormal mucosal pattern, (d) delay in the transit time of the barium column, (e) segmentation of the barium, (f) abnormal position or mobility of the individual segments of the bowel, (g) abnormal peristaltis. The obstructing lesion has been studied with reference to mucosal pattern, general contour and deformity, and behavior during peristalsis. A number of cases of partial obstruction of the small intestine are reported.

FRANZ J. LUST

PATHOLOGY AND LABORATORY RESEARCH

PEPTIC ULCER: THE EFFECT OF ANTICHOLINERGIC DRUGS ON THE MECHANISM OF PAIN: W. L. Palmer, F. Vansteenhuyse, J. B. Kirsner. Am. J. M. Sc. 224: 603-611, (Dec.), 1952.

In 26 experiments in 18 ulcer patients, an acid test was performed before and after the administration of an anticholinergic compound. In 23 of the experiments the anticholinergic drug failed to prevent the induction of pain. The three negative experiments occurred in patients with duodenal ulcer. In one such experiment the procedure was then modified and repeated using a tube in the duodenum; pain developed. Roentgenologic studies using acid barium before and after the administration of the anticholonergic drug, disclosed no direct relationship between pain and gastric or duodenal motility or spasm. It was concluded that anticholinergic drugs do not alter directly the mechanism of pain in peptic ulcer. The relief of pain observed clinically is probably attributable to an indirect effect resulting in decreased exposure of the ulcer to the acid attack.

J. R. VAN DYNE

CONTRIBUTION TO THE STUDY OF STEATORRHEAS: A. L. Froehlich, and N. Buyssens. Acta Gastroenter. Belg. 15:487, (June), 1952.

The clinical features of 12 cases of idiopathic steatorrhea and of 3 cases of lambliasis and 2 cases of anatomical lesions of the small intestines have been described. The diagnosis of steatorrhea is admitted when the percentage of fat in dry feces exceeds 20 per cent: about 70 per cent of the total fat content is hydrolized. The use of an emulsifying agent in three cases had diminished on the average by 16 per cent,

the mean value of fat in dry feces, and increased the amount of hydrolysis by 19 per cent. In half the cases of idiopathic steatorrhea, free hydrochloric acid has been found after histamine stimulation. The amount of choline in the bile from the bile duct is about 110 mg. per cent, that of bile salts is 220 mg. per cent. In three cases of steatorrhea, no choline nor bile salts could be detected in bile from the duodenum. Calcemia is usually low, between 9.5 and 5.4 mg. per cent; phosphoremia is less frequently reduced to between 1.25 and 2.5 mg. per cent. Proteinemia is regularly low. This must be ascribed to a fall of serum albumin. Lipemia is also reduced. The percentage of hyperglycemia after feeding of glucose does not exceed 10 per cent. A fall of blood sugar generally occurs in due course.

After feeding of a fat meal, hyperlipemia does not occur. This may be ascribed to a lack of increase of neutral fat. Cholesterolemia and phosphatidemia increase as usual. The radiological examination of the small bowel discloses either hypotony and hypomotility or increased peristalsis and hypertony. Neither of these aspects can be connected with the severity of the disease. A necropsy has been performed in four cases. The findings disclose a chronic infiltration of the mucosa with mononuclear cells and some fibrosis and also regressive changes in the small intestine.

FRANZ J. LUST

THE RELATION BETWEEN THE PHYSIOLOGIC STIMULATORY MECHANISMS OF GASTRIC SECRETION AND THE INCIDENCE OF PEPTIC ULCERATION: L. R. Sauvage, E. J. Schmitz, E. H. Storer, E. A. Kanar, F. R. Smith, and H. N. Harkins. Surg. Gynec. & Obst. 96:127-142, (Feb.), 1953.

The authors used a total parietal pouch to evaluate the relation of the cephalic, antral and intestinal phases to the development of experimental peptic ulceration. With this preparation of antral phase seems to be predominant. Vagotomy of the pouch does not decrease the incidence of ulceration with this preparation in the dog. It was found, however, that antrumectomy decreased the incidence of ulceration with this preparation in the dog. Antrumectomy and vagotomy combined protect the dog against the development of jejunal (stomal) ulcer.

J. R. VAN DYNE

THE EFFECT OF COBALTOUS CHLORIDE ON THE BLOOD SUGAR AND ALPHA CELLS IN THE PANCREATIC ISLETS OF THE RABBIT: Martin G. Goldner, Bruno W. Volk, and S. S. Lazarus. Metabolism 1:544, (Nov.), 1952.

Pancreas obtained from female rabbits, sacrificed 24 to 48 hours after intravenous administration of cobaltous chloride, showed severe selective damage to the alpha cells. The blood sugar level rose significantly soon after the injection and returned to the normal range within four to five hours. A second intravenous injection of cobalt repeated after 48 hours was followed by a second rise of the blood sugar level. No hypoglycemic levels were encountered after the administration of cobaltous chloride.

FRANZ J. LUST

EFFECTS OF A NEW CHOLINERGIC BLOCKING AGENT (S.K.F.-1637) ON GASTRIC MOTOR AND SECRETORY ACTIVITY: E. C. Texter, G. J. Baylin, C. W. Legerton, and J. M. Ruffin. Am. J. M. Sc. 224:612-618, (Dec.), 1952.

A new cholinergic blocking agent was studied and found to have a potent effect upon both gastrointestinal motility and secretion. The effects on motility is similar to that reported with other cholinergic blocking agents. The changes following parenteral administration were more striking that those noted after oral administration. The drug was found to exert a strong effect on gastric secretion and in five patients achlorhydria was produced. The effects upon secretion appeared to be more striking than had been reported for similar drugs. Side-effects were absent or minimal following the use, however, the role of this drug in the long term management of peptic ulcer is yet to be determined.

J. R. VAN DYNE

BOOK REVIEWS

LES SYNDROMES DOULOUREUX DE LA REGION EPIGASTRIQUE TOMES 1 et 2: Rene A. Gutmann. Fifth edition. Paper covers, 820 and 859 pages respectively with 689 illustrations. Gaston Doin & Cie., Paris, 1951-1952. Price $45.00.

This two-volume text by Gutmann, Roger and Porak has reached a fifth edition. Discussions and numerous illustrations describe clinical forms of epigastric pain, ulcer and other gastrointestinal ailments.

Liver diseases, avitaminosis and its effect on digestive tract diseases are presented in an enlightening manner.

The therapy outlined by the authors may be puzzling, as it differs with those employed in the United States. However, to physicians who are conversant with the French language, the contents of the two volumes will aid them to better understand and treat the painful syndromes of the epigastric area.

FOOD AND NUTRITION: E. W. H. Cruikshank, M.D., Regius Professor of Physiology in the University of Aberdeen. Second edition. 443 pages, illustrated with references at the end of chapters, a table of weights and index. Williams and Wilkins Company, Baltimore, Md., 1951. Price $6.50.

For the physician and dietician dealing with metabolic and nutritional problems, this well written volume will be of material aid. Not only does the author deal with problems of nutrition in Great Britain, but also deals with problems of world malnutrition.

The chapters on vitamins and dietary deficiency diseases, as well as the subsequent chapters contain valuable and informative material.

Although the references are mostly of British source, the reviewer recommends the book as a valuable addition to the library of the physician and dietician.

CLINICALLY IMPORTANT REFLEXES: Dr. Med. Friedrich Wilhelm Bronisch, Instructor, University of Heidelberg, Research Assistant, Psychiatric and Neurologic Clinic, University of Heidelberg. First American edition, revised and enlarged by Clemens E. Benda, M.D., Boston, Mass. 88 pages. Grune and Stratton, Inc., New York, N. Y., 1952. Price $4.75.

This little monograph on reflexes should be very helpful to all medical students, internes, residents and neurologically interested practitioners of medicine.

This book can be a companion volume to the work published by Dr. Robertson of Philadelphia (F. A. Davis Co., 3rd edition) several years ago.

FLUID BALANCE—A CLINICAL MANUAL: Carl A. Moyer, M.D., Professor of Surgery, Washington University School of Medicine, St. Louis, Mo. 191 pages. The Year Book Publishers, Inc., Chicago, Ill., 1952. Price $3.75.

This small monograph aims to present a plain understandable schema of diagnosis pertaining to fluid and electrolyte imbalances and thus is a good guide to the selection of appropriate therapy. An informative review of signs and symptoms association with changes in the body's fluid content and electrolytes is helpfully included.

This book should be of interest to students of the subject and particularly to young surgeons and residents.

THE MERCK INDEX OF CHEMICALS AND DRUGS—AN ENCYCLOPEDIA FOR THE CHEMIST, PHARMACIST, PHYSICIAN AND ALLIED PROFESSIONS: Published by Merck & Co., Inc., Rahway, N. J. Sixth edition. 1167 pages. 1952. Regular edition $7.00. Thumb index $8.00.

This improved sixth edition provides a concise and very comprehensive encyclopedia of drugs and chemicals which is helpful and informative for the student, the druggist, the physician and chemist.

There are a number of tables which add

to the practical usefulness of this new edition. Also, a section for first aid in case of poisoning is found on pages 1145-1157. There is an interesting table of radioactive isotopes used in medical therapy and diagnosis (pages 1108-1111).

This new sixth edition of the Merck index is recommended as a handy helpful volume for all interested in drugs and chemicals.

ISOTOPES IN MEDICINE: Published by Medical Department, British Council. 300 pages. Oxford University Press, New York, N. Y., 1952. Price $3.25.

This excellent review of the various problems concerned with the investigation and use of radioactive isotopes are very satisfactorily considered in this special issue.

Among the contributors are L. H. Gray, S. R. Pele, J. Gross, E. J. Wayne, R. J. Walton, E. H. Belcher, J. W. J. Fay, Henry Seligman and others.

Protein metabolism, thyrotoxicosis, porphyria, malignant effusions are among the subjects concisely and informatively presented.

THE EYE MANIFESTATIONS OF INTERNAL DISEASES (MEDICAL OPHTHALMOLOGY): I. S. Tassman, M.D., Associate Professor of Ophthalmology, Graduate School of Medicine, University of Pennsylvania, Philadelphia, Attending Surgeon, Wills Eye Hospital, Philadelphia, Pa. Third edition. 672 pages with 279 illustrations including 25 in color. The C. V. Mosby Company, St. Louis, Mo., 1951. Price $12.00.

This excellent third edition of a practical work by an experienced ophthalmologist, should be carefully read and studied by all clinicians, internists, residents, internes, medical students, general practitioners, and ophthalmologists. Teachers and instructors in hospitals and medical schools may use this instructive textbook as a guide in a very helpful manner.

The illustrations are good, the subject index of 31 pages is very useful, the printing on good quality paper makes it easy to read.

This work is enthusiastically recommended as the best one volume work on the subject available.

DER DARMVERSCHLUSS UND SONSTIGE WEGSTOERUNGEN DES DARMES: Professor Dr. R. Stich, Gottingen. 188 pages illustrated. Walter de Gruyter & Co., Berlin, 1952. Price DM. 16.80.

In this well written and illustrated book, the author wishes to convey to the reader the nature, diagnosis and treatment of intestinal obstruction.

The literature dealing with this subject is well represented, an unusual procedure in books written abroad. There is also a comprehensive index.

The reviewer suggests that the publishers would find it to their advantage to have this little volume translated into other languages.

THE EARLY DIAGNOSIS OF THE ACUTE ABDOMEN: Zachary Cope, B.A., M.D., M.S., Lond., F.R.C.S., Eng., Consulting Surgeon to St. Mary's Hospital, Paddington and to the Bolingbroke Hospital, Wandsworth Common, Late Hunterian Professor, Arris and Gale and Bradshaw Lecturer, Royal College of Surgeons. Tenth edition. 270 pages. Geoffrey Cumberlege, Oxford University Press, New York, N. Y., 1951. Price $3.50.

The first edition of this practical and informative little volume appeared in 1921, the ninth edition appeared in 1945 and now the tenth improved edition is available. This work is a report of the author's own experience. In the nineteen chapters, the author ably and authoritatively discusses the principles of diagnosis in acute abdominal disease, methods of diagnosis, history, examination, etc., appendicitis, gastric and duodenal ulcer, acute pancreatitis, acute intestinal obstruction, intussusception, cancer of the large bowel, volvulus, strangulated and obstructed herniae, ectopic gestation, cholecystitis, acute peritonitis, abdominal injuries, etc.

The reviewer found this work interestingly instructive.

SIGNS AND SYMPTOMS—APPLIED PATHOLOGIC, PHYSIOLOGY AND CLINICAL INTERPRETATION: Edited by Cyril M. MacBryde, A.B., M.D., F.A.C.P. Second edition. 783 pages with 26 contributors, 98 illustrations, 50 charts and 8 color plates. J. B. Lippincott Company, Philadelphia, Pa., 1952. Price $10.00.

Not only is this volume a veritable physical diagnosis, but it is also a volume which the student and the practitioner will value more and more as he reads the interesting and informative material contributed by the outstanding clinicians.

In the introduction by the editor, Dr. MacBryde, the reader will be rewarded by the numerous salient points dealing with the history taking and its graphic relation to the interpretation of the symptoms as given by the patient.

The reader perusing the chapter relating to pain will undoubtedly apply the knowledge gained from the text in his next case. The chapter on sore tongue and sore mouth, as well as thoracic and abdominal pain is well written and clearly presented.

All in all the book is an excellent treatise and medical students, general practitioners as well as physicians in the various specialties, will find it of great value. It is highly recommended.

BIOLOGICAL ANTAGONISM—THE THEORY OF BIOLOGICAL RELATIVITY: Gustav J. Martin, Sc.D. 516 pages, illustrated. Blakiston Company, Philadelphia, Pa., 1952. Price $8.50.

Gustav J. Martin has written a truly remarkable volume on practical biochemistry and pharmacology.

The casual student of biochemistry will find this book far advanced for practical purposes. However, the research worker will be rewarded by the newer concepts elucidated by the author.

AMBULATORY PROCTOLOGY: Alfred J. Cantor, M.D., with a foreword by Beaumont S. Cornell, M.D. 563 pages, 382 illustrations, bibliography and index. Paul B. Hoeber, Inc., New York, N Y., 1952. Price $10.00.

This is the second edition of Ambulatory Proctology in six years and neither the author nor the publisher spared expense in preparing this volume. The paper is excellent, the type is clear, and the illustrations are beautiful and self-explanatory.

The author calls attention to the many new advances in treatment both medically and by surgery which have been innovated in the past five years and the reviewer agrees with him that in this excellent text the general practitioner as well as the specialist will find simple and logical suggestions dealing with diseases involving the anorectal area.

The reviewer recommends Dr. Cantor's Ambulatory Proctology as a must.

PHYSIOLOGIE UND PATHOLOGIE DES BILIRUBINSTOFFWECHSELS ALS GRUNDLAGEN DER IKTERUSFORSCHUNG: Dr. Med. et Phil. Habil. Tr. Baumgartel, Munchen mit 2 Abbildungen. 271 pages, George Thieme Verlag, Stuttgart, Germany, 1950. Price 27 D.M.

This monograph should be of considerable interest to all gastroenterologists, physiologists and clinical pathologists and biochemists and to medical students and instructors. The reviewer recommends that this work by Dr. Baumgartel be translated into English so that a larger number of readers would be able to gain the information contained in this monograph. The reviewer was also interested in the historical section—"Zur Historischen Entwicklung des Ikterusproblems" (pages 7-32).

There is an authors' index of 8 pages and a subject index of 9 pages, which adds to the value of the monograph.

SYNOPSIS OF PATHOLOGY: W. A. D. Anderson, M. A., M.D., F.A.C.P., Professor of Pathology, Marquette University, School of Medicine, Pathologist, St. Joseph's Hospital, Milwaukee, Wisc. 788 pages with 334 text illustrations and 13 color plates. Third edition. The C. V. Mosby Company, St. Louis, Mo., 1952. Price $8.00.

The author of this improved third edition is a trained pathologist and teacher of the subject.

Numerous changes and additions have been incorporated in this new edition, including many of the recent advances in the

knowledge of many of the conditions presented in this practical work. Among those who helped the author are Dr. Henry Pinkerton and Dr. Robert L. Kascht.

The illustrations for the most part are good and quite instructive. Many references to the literature follow the various sections. This is a helpful synopsis of pathology and should be readily available in all medical school libraries and hospital libraries. All medical students, internes, residents and busy general practitioners will find much useful information in readable, concise, adequately presented manner in this compact little volume. It is recommended for daily use by junior and senior medical students.

THE OLD EGYPTIAN MEDICAL PAPYRI: Chauncey D. Leake, Ph.D., University of Texas, Galveston Branch, 108 pages. University of Kansas Press, Lawrence, Kansas, 1952. Price $2.00.

Of fascinating interest to the medical historian, are the eight Egyptian Medical Papyri which Dr. Leake has studied very carefully during recent years.

Although Professor Leake is primarily a pharmacologist, he is also a well-known medical historian and "Medical Egyptologist".

Professor Leake reviews these papyri and gives an interesting survey of weights and measures and the therapeutics as found in these ancient writings, particularly the Hearst document. This interesting little volume of 108 pages will be appreciated by medical historians and students interested in ancient therapeutics and measurements.

TEXTBOOK OF SURGERY: Edited by H. F. Moseley, M.A., D.M., M.Ch. (Oxon), F.A.C.S., F.R.C.S. (Eng.), F.R.C.S. (C), Assistant Professor of Surgery, McGill University, Associate Surgeon, Royal Victoria Hospital, Montreal, Canada, with a foreword by G. Gavin Miller, M.D., C.M., M.Sc., F.R.C.S. (C), F.A.C.S., Chairman of the Surgical Department, McGill University, Surgeon-in-Chief, Royal Victoria Hospital, Montreal, Canada. 896 pages with 160 text illustrations and 16 color plates. The C. V. Mosby Company, St. Louis, Mo., 1952. Price $15.00.

This new textbook of surgery has been compiled and well written by Canadian contributors from the Royal Victoria Hospital and McGill University. The book is dedicated to Dr. G. Gavin Miller, who contributes the foreword. The two column arrangement, good quality paper, and clear type make for easy reading.

The colored plates are mostly duplicated from Ciba publications and the American Cancer Society publications. They are too highly colored in most instances and quite unusual for a textbook.

This new addition to an already good list of excellent textbooks of surgery that have appeared in recent years, will not be received with much enthusiasm and praise. However, the book will be helpful and quite instructive to medical students, internes and residents.

OUTLINES OF INTERNAL MEDICINE: Edited by C. J. Watson, M.D., Head, Department of Medicine, University of Minnesota. Seventh Edition. First Printing. Wm. C. Brown Company, Publishers, Dubuque, Iowa, 1952. Price $13.00.

There are five parts in this 1952 edition: Infectious Diseases, Diseases of the Blood and Blood forming Organs, Congenital Heart Diseases, Deficiency Diseases, Clinical Chemistry and Microscopy.

Among the contributors to this volume are W. W. Spink and W. H. Hall, J. A. Myers, T. Lowry, A. A. White, C. J. Watson, Ben Heller, R. V. Ebert and A. C. Kerkhof (Electrocardiography). The section on "Diseases of the Liver and Biliary Tract" is by C. J. Watson and V. W. Hoffbauer. Samuel Nesbitt contributes "Diseases of the Pancreas". "Diseases of the Mouth, Esophagus, Stomach and Duodenum" was contributed by J. B. Carey. Reuben A. Johnson prepared the section on "Diseases of the Small Intestine, Colon and Rectum". Dr. M. J. Shapiro, the experienced cardiologist, has written the informative and helpful section on "Congenital Heart Diseases". Dr. C. B. Chapman's contribution on "Arterial Hypertension and Dr. Richard Ebert's section on "Arteriosclerosis of the Coronary Arteries and Angina Pectoris" are instructive and adequate.

This type of textbook is helpfully useful for all medical students, internes, residents and general practitioners and is recommended by this reviewer.

MODERN TRENDS IN GASTROENTEROLOGY: F. Avery Jones, M.D., F.R.C.P., Consultant in Gastroenterology to the Postgraduate Medical School of London, England; to St. Marks Hospital and the Royal Navy. 831 pages, numerous illustrations, line drawings and tables. Paul B. Hoeber, Inc., Medical Book Department of Harper Bros., New York, N. Y., 1952. Price $20.00.

The author has an array of talent which would be of credit to an encyclopedic compilation. There are thirty-four well written and edited chapters with beautiful roentgen illustrations and specific explanations. Here and there one finds typographical errors in spelling, like "sclerodermia" instead of "scleroderma", but this does not detract from the clear and well printed text on coated paper in the Hoeber style.

The editor of this instructive volume has scanned the world literature and includes American and other references from countries outside of Continental Europe.

Congratulations are due Dr. Jones and the publishers, for bringing out a volume of this type. Is is recommended that clinicians place this reference book on their desks rather than on the book shelf.

THE LIVER: Kasper Blond, M.D., and David Haler, M.B. 268 pages, illustrated in black and white with an extensive bibliography and index. The Williams and Wilkins Company, Baltimore, Md., 1950. Price $5.00.

In this well written and documented book, the interested reader will find material which ordinarily is not found in the literature and many of the books dealing with liver disease.

Glancing over the contents, the reviewer noticed that in the seventeen chapters the authors have correlated the sequelae caused by the liver and its arterial and venous system. On page 134, the authors state, "Appendicitis, like cholecystitis, pancreatitis and nephritis are either acute, chronic or recurrent and begin with inflammation and that they are caused by venous congestion in the portal roots draining the organs involved". Colicky pain is not caused by mechanical abnormalities such as kinking or fecoliths, but rather is a typical sign of acute portal back pressure.

One page 136, the reviewer found interesting reading referable to angina pectoris. Other chapters deal with asthma, goiter, hemorrhoids, anorectal mucosa and varicose veins of the leg.

It is a useful and informative little volume and is recommended for the physician's library.

PROGRESS IN CLINICAL PSYCHOLOGY: Edited by Daniel Brower, Ph.D., Lawrence E. Abt, Ph.D. 328 pages, Volume I (Section I). Grune & Stratton, Inc., New York, N. Y., 1952. Price $5.75.

This is an informatively interesting volume. The editors have included their chapters, and the articles by well-known psychologists. Of interest, are the chapters on "Testing for Psychological Deficit"; "The Rorschach"; "Thirty Years After"; "Group Psychotherapy" and "The Emergence of Clinical Psychology".

Students of psychology, psychologists, and instructors, and physicians interested in this subject, will find this volume helpfully instructive.

A MANUAL OF PARASITOLOGY FOR MEDICAL STUDENTS AND BEGINNERS: Mark M. Shapiro, M.D., M.S., Fellow, Royal Society Tropical Medicine and Hygiene, London, Fellow, International College of Surgeons, Consultant in Tropical Medicine and Parasitology, American Hospital, Chicago, Ill. Foreword by Sir Philip Manson-Bahr. 140 pages. Grune & Stratton, New York, N. Y., 1951. Price $5.50.

This little monograph should be helpful to students and to beginners and young practitioners, internes and technicians. Among the topics covered are malarial parasites, intestinal protozoa of man, trematodes, schistosomes, nematodes and cestodes, diphyllobothrium latum, taenia solium, taenia saginata, echinococcus granulosus (hydatid) and hymenolepis nana.

There is a closing chapter (XIV) on "Diagnostic Methods in Parasitology". Appendix I and II, and a short bibliography.

DIABETES INSIPIDUS: Harry Blotner, M.D., Associate Visiting Physician, Beth Israel Hospital, Boston, Mass. Edited by Henry A. Christian, A.M., M.D., LL.D., Sc.D. (Hon.), M.A.C.P., Hon. F.R.C.P. (Can.), D.S.M. (A.M.A.), (Reprinted from Oxford Looseleaf Medicine with same page numbers as in that work). 206 pages. Oxford University Press. New York, N. Y., 1951 $4.50.

This monograph on Diabetes Insipidus by a student of the subject is well written and easily understandable. An excellent history is included. Both Galen and Aretaeus used the term diabetes. Galen may have seen two cases of diabetes insipidus and Aretaeus described diabetes.

Sir Thomas Willis is credited by some writers (1674-1684) as the first to differentiate diabetes mellitus from diabetes insipidus but Blottner questions this priority and doubts that Willis separated these two conditions.

W. Cullen in 1789 first used the names of these two types of diabetes. The physiology of diabetes insipidus and pathology are well discussed. Symptoms and laboratory studies, diagnosis and treatment are satisfactorily presented.

An exhaustive bibliography of 470 references completes the work.

This monograph is an authoritative work on diabetes insipidus.

DIAGNOSTIC ELECTROENCEPHALOGRAPHY: Hans Strauss, Mortimer Ostow, Louis Greenstein. With a foreword by Leo M. Davidoff. 282 pages. 46 illustrations. Grune & Stratton, New York, N. Y. 1952. Price $7.75.

This book addresses itself to the medical student, the physician who wants to be informed about the basis, practical application and diagnostic value of electroencephalography, as well as to the specialist who wants to apply this method himself.

The first part deals with general aspects of the electroencephalogram, beginning with a history, the equipment and the recording method. It goes on to describe the components of the record, constituting normal and abnormal electroencephalograms. The physiology of the electroencephalogram, its changes accompanying psychic function and metabolic alterations are treated in special chapters. Characteristics of the normal electroencephalogram in adults and children are discussed and a classification of various types of abnormal electroencephalograms is presented.

Part II describes the types of electroencephalograms occurring in patients with various disorders, not only those with primary diseases of the nervous system, but also those with disorders arising outside the nervous system and with exotoxic disturbances. A special chapter is dedicated to the disturbances of the carbohydrate metabolism including hypoglycemia, relative hypoglycemia, diabetes and posthypoglycemic encephalopathy. The electroencephalogram in mental disorders, including the psychoneuroses and psychosomatic disturbances, is dealt with in detail.

The third part is dedicated to the diagnostic evaluation of the electroencephalogram. This part is of particular value to the physician who wants to know whether the electroencephalogram will be of value to him in solving a particular diagnostic problem. Tables show clearly in which conditions normal or certain types of abnormal records can be expected.

There is an extensive bibliography. Forty-six illustrations show the various types of records.

This book is distinguished by the clarity and simplicity of the presentation of a subject which is still relatively young and which many of us have not approached because there was no short and systematic presentation of the subject. The lack of such a presentation is no longer an excuse after this book is available. We agree fully with Dr. Davidoff, who says in the foreword: "In this book, based on many years of experience, with a very large and diversified clinical material, Drs. Strauss, Ostow and Greenstein have shown us the boundaries of this field, and presented us with the tools to explore it to the limits."

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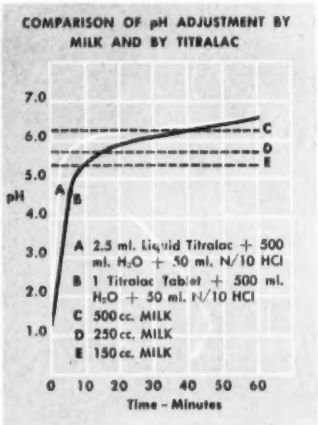

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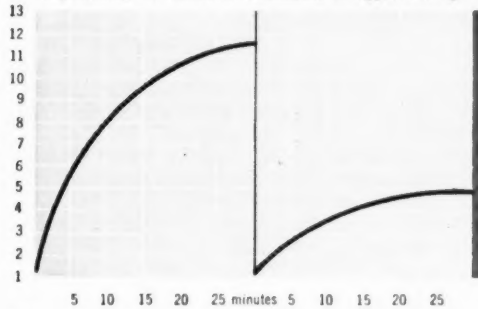

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1. *Woldman, E. E.:* Am. Jour. Med. Sc., 194:333, Sept., 1937.
2. *Smith, F. H.:* Gastroenterology, 8:494, Apr., 1947.

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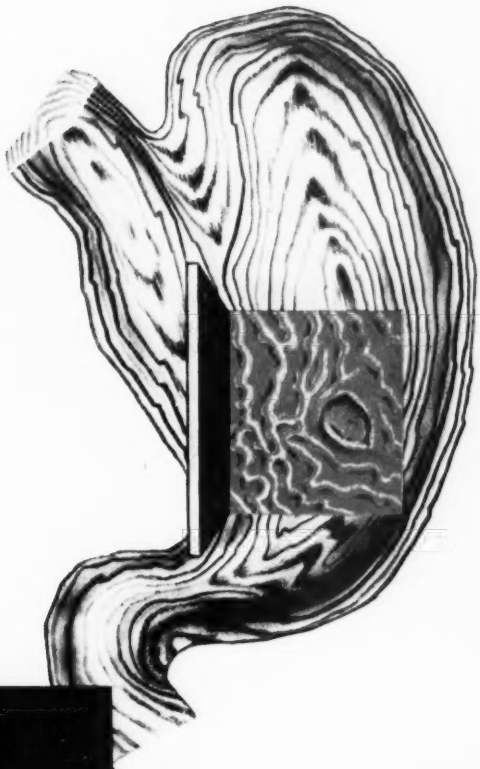

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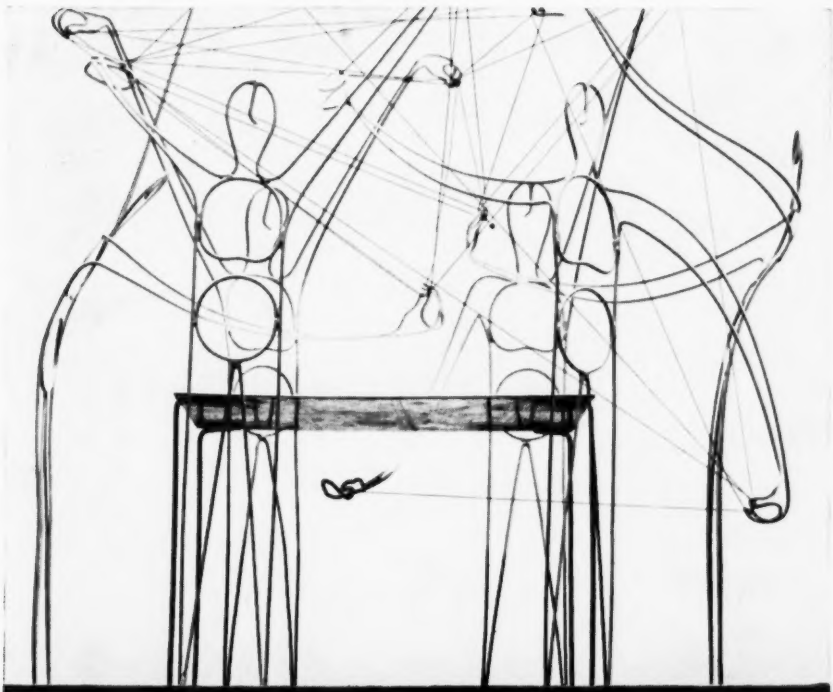

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